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Issue 23

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To our readers: We are working in a large number of highly technical, specialized areas for which adequate Russian-English glossaries have yet to be compiled. We ask your help in improving the accuracy and specificity or our English terminology. Please fill out the form below whenever you encounter an incomprehensible, incongruous, awkward or otherwise inappropriate term. While we solicit all suggestions for improved renderings, the statement that a term is inappropriate provides us with useful information, even when no better alternative can be suggested. A copy of this form will appear in all future issues of the Digest. Thank you for your help.

Abstract Number	Incorrect or inappropriate term	Suggested rendering

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FROM THE EDITORS

This is Issue 23 of the USSR Space Life Sciences Digest. Of particular interest in this issue are abstracts of 16 sections from a Soviet book on mammalian ontogeny in weightlessness and a translated article on biomedical support of manned flights to Mars. The following abstracts present or discuss Soviet space flight data: Life Support Systems Special Feature, Musculoskeletal System P 1065; Reproductive System P1042-1056, 1058.

Anyone wishing copies of tables or figures referred to but not reproduced in the Digest should contact us at the address below.

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ADAPTATION

P1086(23/89) Simonov PV.
Issues in ecological physiology
Text of paper presented at the General Meeting of the Physiology Division of the USSR Academy of Sciences, December, 1988.
In: Uspekhi Fiziologicheskikh Nauk.
20(2): 113-115; 1989.
[No references]

KEY WORDS: Adaptation, Biospherics, Ecological Physiology, Space Medicine, Habitability and Environmental Effect, Extreme Conditions

Text: The discipline of ecological physiology studies the mechanisms through which human health and work capacity are maintained in the face of a broad range of changes in the natural environment. Humans are unique in that they are simultaneously the agents and the subjects of the effects they themselves produce in the environment. This creates a difficult conflict between the long-term biological and cultural/historical needs of humans as biosocial entities and their drive for social [i.e., economic] development, the satisfaction of which often has [ecological] consequences that are unforeseen or ignored. It has recently become obvious that it is vitally important to humanity that these two types of needs be reconciled in a way that strictly accords with mankind's priorities.

Physiology, including human psychophysiology, is the area where these two opposing tendencies conflict in the most obvious way. Thus, humans have enormous adaptive capacities, including the ability to adapt to factors which they have never encountered in the course of their evolution, for example, weightlessness during space flight. I should note here that physiological studies of the effects of weightlessness on the body have served as the basis for a system of prophylactic countermeasures making it possible to increase the duration of space flights to a year, and in the future even longer.

However, human capacities to adapt have the insidious property of masking the adverse influence of environmental factors for a certain period of time, so that harmful effects are discovered only after a delay. This is why one of the most urgent goals of ecological physiology is to determine the points at which adaptation becomes merely a temporary compensation for a physiological injury. We are very fond of extolling the omnipotent "reserves" of the human body, including the reserves of the brain, and of calling for the mobilization of these reserves, which hold promise for increasing physical and intellectual capacities (memory, learning, etc.) But, perhaps, nature was wiser than we are when she provided humans with an untouchable reserve capacity to be saved for the occurrence of truly extreme conditions. Perhaps we are wrong to attempt to use extraordinary artificial measures to "extract" these famous reserves from humans for routine use. It is clear that only meticulous study of nature, of the long period during which our reserve capacities developed, will enable us to overcome the limits on their rational use.

In general, the fact that we are ignorant of or have chosen to ignore the real needs of humans causes some of our social (economic) actions to have unexpected consequences. For example, the drastic change in working and living conditions in the Far North, including measures taken with the best of intentions, has led to such undesirable consequences as increase in suicide and alcoholism among the native populations. Separation of children from their parents (through placement in boarding schools) has resulted in fewer members of the indigenous population returning to their families homes, remaining instead in more densely populated areas creating a number of ecological and demographic problems.

The facts indicate that the solution to certain of these problems is not possible without the participation of physiologists. Thus, analysis of the hemispheric dominance in the brain of members of the indigenous populations of the Far North showed that as many as 70% show predominance of the right brain (spatial-imaging) type of perception and information processing. As a result, the school curriculum, which is traditionally oriented to the logical-verbal type of perception and information processing, is relatively ineffective for teaching children of the indigenous population. This leads to the the mistaken belief that these children are relatively slow. It has also been shown that one of the reasons for the increased disease rate in members of the indigenous, as well as the more recent, populations of these regions is certain characteristics of the immune function, amounting to a condition of relative immune deficiency.

I want to emphasize that only the use of rather complex modern methods of physiological research has allowed us to obtain reliable data about the acceptable and dangerous effects of a large number of ecological factors. Thus, evaluation of the reactivity of portions of the brain (on the basis of parameters of their electrical potentials during visual stimulation of a number of types) suggests that there may be substantial shortcomings in the illumination of work sites in many enterprises of our country, leading to fatigue and eye strain. The systematic study of saccadic eye movements has allowed us to discover the negative effects of homogeneous (i.e., monotonous, unchanging) visual backgrounds, and to formulate concepts of video-ecology as an area of human ecological physiology.

Other studies have demonstrated the truly dramatic effects of noise on brain activity, as manifested by stable changes in electrical activity and decreased tolerance of factors conducive to neuroses. Electron microscopic analysis has revealed changes in the microstructure of nerve and glial cellular elements of the auditory cortex that occur after long-term exposure to noise. The biological effects of artificial electromagnetic fields are also in need of further study. The absence of thresholds and the cumulative nature of the effects of this particular factor will not mask its true ecological significance indefinitely.

As early as 1965, using the EPR method, Soviet authors established the reason why hypoxia occurs in response to certain doses of nitrites and nitrates, the unfortunate consequences of the use of which in agriculture and the food products industry are now so widely known.

The need for industrial activity under the unfamiliar conditions of polar, subpolar, and desert zones, at high altitudes and under water, and under conditions of increased emotional strain necessitate the development of objective methods for assessing human functional status and work capacity under these conditions. This must be accomplished if we are to develop scientifically justified guidelines for generating schedules for work and leisure, and creating rational approaches to occupational selection and prevention of undesirable consequences, including those of emergency situations. In 1987, the scientists of the Institute of Higher Nervous Activity and Neurophysiology of the USSR Academy of Science, jointly with the N. N. Burdenko Institute of Neurosurgery of the USSR Academy of Medicine, proposed a set of methods for diagnosing and predicting the functional status of the human brain with application to the requirements of labor psychophysiology and clinical medicine. These methods were successfully tested in actual industrial workplaces and were evaluated positively by the appropriate specialists.

A constructive solution to the problem of analyzing the effects of a set of industrial ecosystem factors on humans was proposed in Belorussia. Scientists of the Institute of Physiology of the Belorussion Academy of Sciences, in collaboration with medical personnel of the republic, developed an apprach to ecological physiological monitoring of the major physiological human functions in ecosystems encompassing heterogeneous industrial activities.

Their approach had two interacting parts. First, they envision experimental research with the goal of finding the physiological mechanisms underlying the effects of physical and chemical factors arising from industrial production. Secondly they proposed the use of a "health passport" for various groups of the population and study of the state of the major functional systems, the organs of circulation, respiration, digestion and the immune system. The new collaborative approach would integrate physiologists and clincial personnel into a single work group and would require large industrial concerns to contribute financially.

To help with this project, a special computer laboratory for processing data from mass examination of certain portions of the population is being set up and staffed. The program also calls for training physiological ecologists and ecological physicians in the higher educational institutions of Belorussia.

With the help of just of few of the possible examples, I have tried to show that ecological physiology must be given an important place in the system of ecological research, since it is this field which will be able to assess the acceptability of interactions between humans and particular environmmental factors. It is clear that physiology will be able to perform such tasks only if it is provided with modern experimental technology, instruments, and reagents. In the past, the electronic apparatus we have used in our experiments had generally not been produced by Soviet industry. For decades we have been using imported apparatus and imported apparatus alone. The stringent limitations on transactions in foreign currency have created an impasse, from which for the present I can see no way out. Furthermore, even continued utilization of what imported apparatus we do possess is threatened by the impossibility of obtaining replacement parts. What apparatus we will use tomorrow remains unclear.

At the general Meeting of the Division of Physiology in December of this year we considered many aspects of the issue of the possible participation of physiological institutes of the Division, scientific centers, and republic Academies in a program devoted to "Human Ecology." A resolution was adopted to organize a section on ecological physiology within the Scientific Council of the USSR Academies of Science and Medicine on Physiological Sciences, which will be responsible for coordinating the appropriate physiological and biomedical research.

PAPERS:

P1059(23/89)* Ponomarenko VA, Lapa VV.
Using information to control pilot reliability under extreme performance conditions.
Kosmicheskaya Biologiya i Aviaskosmicheskaya Meditsina.
23(2): 16-21; 1989.
[13 references; none in English]

Aviation Medicine, Human Performance, Psychology
Humans, Pilots
Psychology, Information, Perception, Flight Representation

Abstract: The authors argue against the traditional approach to pilot reliability, which, they say, treats functional state as if it is the sole determinant of this characteristic. They cite two experiments that suggest otherwise. In one, pilot state was altered either positively or negatively by posthypnotic suggestion or administration of drugs. Any alteration in pilot state, whatever its direction, led to decreased reliability in a secondary signal detection task by increasing false alarms. In the second experiment, after long performance of a monotonous task, pilots were observed to initiate behaviors (singing, thinking of other things, etc.) that improved functional state, but actually worsened performance on a vigilance task. On the other hand, measures that provided additional information, by improving the pilot's internal representation of his task situation, improved vigilance. The authors argue that supporting the coherence of the pilot's mental "flight representation" is an important factor in improving performance reliability, regardless of functional state. However, most measures developed in aviation medicine to improve reliability have focussed on functional state (exercise programs, autogenic training, pharmacological preparations, stimulation of biologically active points, electrostimulation of muscles and others).

The authors propose to develop a similar series of measures directed at providing the pilot with an optimal psychological representation of the flight under extreme conditions. These measures, they claim, will improve the pilot's state by improving his performance, rather than vice versa. Experiments simulating emergency situations have demonstrated that a pilot's emotional state and behavior can be altered by varying the completeness and clarity of the information provided him. Given the same [simulated] threat to flight safety, pilots provided with clear information showed minimal changes in autonomic parameters, while pilots provided with vague or contradictory information displayed major changes. Errors in perception and thinking, and breakdowns in performance in simulated situations were generally associated with vague or contradictory information rather than with threats to performance success. The authors conclude that provision of complete and clear information about extreme situations, by facilitating rapid formation of an appropriate internal representation, are an important means for preventing emotional stress and thus increase reliability.

Additional studies have shown that verbal information can also help the pilot to rapidly and veridically represent an emergency situation. It has been found that short instructions (a plan of action) improve reliability in situations where the nature, number, and order of operations vary as a function of the conditions and flight mode. In other situations such instructions do not affect reliability.

The use of computers on board aircraft has great potential for providing information to facilitate pilots' internal representations of flight conditions. It has been found that such information, presented verbally, can help a pilot form a veridical representation while he

is suffering from various illusions, i.e., relying on non-veridical sensations. One future trend the authors foresee is the creation of adaptive information display systems, the properties of which (content, size, rate, spatial parameters) would change to compensate for external or internal factors that tend to disrupt performance. On-board computers could make such systems possible. The authors have experimented with adaptive changes in brightness and angular dimensions of symbols on an electronic display screen as a means of increasing reliability of information perception in subjects exposed to acceleration. At acceleration of 7-8-G, subjects could hold a target within the acceptable zone three times the normal period when the visual contrast of displayed symbols was increased from 1.5 to 9. Time required to detect a symbol on the screen in noise, the secondary task, was decreased by 30%. Brightness could be increased or other display properties made more salient to compensate for incrasing acceleration or worsening pilot physiological state. The authors acknowledge that a great deal of work must be done before linkage of display systems to parameters of pilot functional state can be developed for actual use.

Figure 1: Probability of detecting deviations from set values of flight parameters

Figure 2: Ratio of energy among EEG waves during various stages of flight

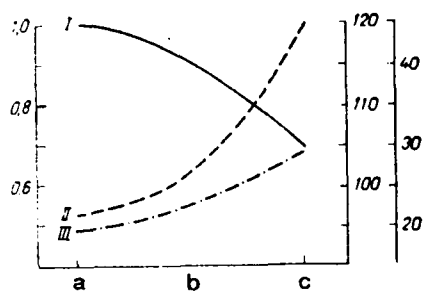

Figure 3: Reliability of performance and autonomic parameters in simulated emergencies as a function of nature of information:

a - clear information; b - vague information; c - contradictory information; I - probability of effective action; II - heart rate/minute; III - respiration rate/minute.

PAPER:

P1089(23/89) Doroshenko NM, Korpachev VV.
The role of the spleen in regulation of plasma calcium under normal conditions and during stress.
Fiziologicheskiy Zhurnal.
35(1): 17-21; 1989.
[15 references; 2 in English]
Authors' Affiliation: Kiev Institute of Endocrinology and Metabolism; Ukrainian Ministry of Health

Body Fluids; Calcium Homeostasis
Rats; Chinchilla
Spleen; Splenectomy; Splenin; Stress; Exercise

Abstract: This study investigated the effects of splenectomy on blood calcium in different animal species, the effects of stress associated with physical exercise on blood calcium in normal and splenectomized animals, and the effects of spleen extract on this parameter. Three experiments were performed on a total of 198 male rats and 38 male chinchillas. Plasma calcium was measured spectrophotometrically. The first experiment measured CA^{2+} concentration in the blood of rats and chinchillas on days 5, 10, and 15 after splenectomy. The second experiment observed the effects of stress (forced swimming for 1-5 hours) on intact and splenectomized rats. The third investigated effects of administration of splenin in various concentrations on blood calcium of normal rats and rats exposed to stress. In all experiments splenin was injected parenterally in doses of 0.25 ml/100 g in differing dilutions (1:10; 1:50; 1:100) of saline. Concentration of calcium was measured 5, 10 and 15 days after operations. Control animals also were operated on, but the spleen was not removed. Results were tested statistically using Student's t.

It was found that in both species studied, splenectomy led to an increase (by a factor of 3 for rats and 2 for chinchillas) in blood calcium by day 15. The stress reaction engendered by intense physical exertion led first (hour 2) to a decrease in blood calcium and then to an increase. Animals which, 15 days previously, had been splenectomized, leading to an increase in plasma calcium, showed even further increases associated with exercise stress. These increases were evident virtually immediately and were sustained until the end of the treatment. Administration of splenin (extract from the spleens of cattle) lowers blood calcium when given in low doses, but does not affect this parameter in higher doses. Administration of splenin before exercise (particularly in low doses) helped to normalize blood calcium. Administration of splenin to splenectomized animals forced to swim also normalized calcium in plasma. These results are interpreted as supporting the hypothesis that the spleen participates in calcium homeostasis and as suggesting that the mechanism underlying this participation is humoral.

Table 1: Dynamics of plasma calcium in splenectomized animals

Table 2: Dynamics in plasma calcium in intact and splenectomized animals exposed to stress

Table 3: Effects of administration of splenin in various doses on the concentration of calcium in normal animals exposed to stress

PAPERS:

Assessment of effects of a single exposure to ammonia on photosynthesis of lettuce plants in an airtight phytotron.

Kosmicheskaya Biologiya i Aviaskosmicheskaya Meditsina.
23(2): 67-70; 1989.
[16 references; 7 in English]

Botany, Photosynthesis
Lettuce
Habitability and Environmental Effects, Air Pollutants, Ammonia, Hermetically Sealed Spaces

Abstract: The problem of evaluating the effects of air pollutants on higher plants has attracted attention in connection with the experimental discovery that growth and development of plants are inhibited in an inhabited airtight environment. The present work attempted to evaluate the threshold of the phytotoxic effect of ammonia in concentrations of 10-20 mg/m^3 in a single 2-hour exposure of lettuce plants. Subjects were head garden lettuce plants, aged 28-32 days, at the end of the vegetation stage. This is the age at which lettuce plants show the maximum growth rate which is usually correlated with maximum sensitivity to pollutants. The experimental and control colonies were cultivated without a substrate, using the subirrigation method in two identical airtight phytotrons with stable atmospheric temperature and humidity, concentrations of CO_2 and O_2, exposure to photosynthetically active radiation, rate of air flow, pH, temperature and composition of the nutrient medium. Apparently ammonia concentrations used were 10, 15, and 20 mg/m^3. Parameters measured included rate of increase in concentration of oxygen in the phytotron (a general index of photosynthesis). Other parameters reflected the state of the most sensitive systems of the plant: *viz.*, rate of photosynthetic electron transport, rapidity of the Hill reaction, and degree to which the chloroplast membrane was energized when the leaf was illuminated. The chloroplasts of the lettuce leaves were isolated and the speed of the Hill reaction with 2,6-dichlorophenolindophenol was measured in a suspension of chloroplasts spectrophotometrically as well as by dynamic redox-potentiometry. Effects on electron transport were measured on the thylakoid membrane on the basis of the electrochromic shift of the absorption band of carotinoid pigments and chlorophyll based on photoinduced changes in optic absorption at 520 nm as compared to 490 nm in normal leaves. To measure energization of the chloroplast membrane, the ratio (α) of the amplitude of the rapid phase of decreased absorption in response to extinguishing a light, to the amplitude of the rapid phase of increased optic absorption when the light was turned on was computed. The difference 1-α, which reflects the difference in concentrations of protons between the internal and external spaces of the thylakoid when illuminated, increases to 1 when there is maximum bonding and falls to 0 when there is disassociation.

All parameters of photosynthesis decreased during fumigation and then normalized after exposure over the course of 2-3 days. All parameters showed a similar pattern of change suggesting that the observed decrease in gas exchange may be due to the inhibiting effect of ammonia on photosynthesis. If a 10% decrease in rate of photosynthesis is taken as threshold for unacceptable phytotoxic effects, a 2-hour dose of 20 mg/m^3 with a 28-day culture was found to be the threshold dose.

Table: Pattern over 3 days of changes in rate of visible photosynthesis from the start of 2-hour exposure of plants to an atmosphere containing various concentrations of ammonia

Figure 1: Photoinduced changes in optic absorption of a lettuce leaf at wave length of 520 nm relative to 490 nm

Figure 2: Difference in photosynthesis between the control colony and the experimental colony exposed for 2 hours to an atmosphere containing various concentrations of ammonia

Figure 3: Diagram of loss of photosynthetic productivity of lettuce plants exposed to various concentrations of ammonia

P1072(23/89)* Brill' OD, Borzunov VB, Vikhrov AI, Vorob'yeva NG, Ivanov LI, Kovalev YeYe, Yanushkevich VA.
The combined effects of β-radiation and shock waves on lettuce (Lactuca sativa L.) seeds.
Kosmicheskaya Biologiya i Aviaskosmicheskaya Meditsina.
23(2): 70-74; 1989.
[17 references; 6 in English]

Gemination Rate, Anomalous Development
Lettuce; Seeds
Radiobiology, Heavy Ions; Shock Waves; β-Irradiation

Abstract: Damage from heavy ions in space has not been limited to ionized losses along the impact track. One possible mediator of the additional effects may be the shock and heat waves arising from the impact. The shock wave may also have a modifying effect in the δ -electron "coat" ("envelope"?) of the heavy ion tracks. This work studied the sequential effects of shock waves and β-radiation, simulating shock waves from the track of heavy charged particles and their δ-electron envelope, on lettuce seeds. To model the shock waves from heavy charged particles, air-dried lettuce seeds were irradiated with a flat shock wave with pressure amplitudes of 100, 200, and 600 MPa, generated by a 50-nsec laser impulse with energy of ≈15 J. in a thin opaque layer of black enamel 1 cm^2. The seeds were attached in such a way (using trace quantities of modeling clay) that virtually all of them were free and were oriented perpendicular to the wave front so that the wave fell in the most sensitive area -- the apical meristem of the root. This made it possible to irradiate 30 to 40 seeds at a time. Seeds were irradiated in water, with the biostack in the water for 2-3 minutes, after which it was placed on filter paper and dried. Effects of δ-electrons were simulated using β-irradiation from $^{90}Sr+^{90}Y$ in a dose of 100 Gy. The seeds were either exposed first to the shock wave and then to the β-radiation or vice versa to study the effects of treatment sequence. The interval between the two treatments was 24 hours.

Seeds began to sprout in significant numbers 20 hours after the final treatment. Observation period was 270 hours. In some conditions black bands of necrosis were noted in the swelling seeds, localized in the cotyledon, rootlets, or the area between them. These strips were associated with anomalous development. Such bands were absent in the control conditions, in seeds exposed only to shock waves of 100 MPa, or such waves combined with β-irradiation, or β-irradiation alone. No differences in distribution of the bands were noted in seeds exposed to the same levels of shock waves, but the breadth of the bands increased as the amplitude of shock wave increased. The germinating ability of seeds exposed to shock waves of 100 MPa and then irradiated with β-rays showed little difference from the control and approached 100%. After exposure to shock waves 200 MPa in amplitude sprouting was retarded and the number of abnormally developing plants increased significantly, composing nearly half the sprouts. However, at this amplitude there was no significant decrease in germinating ability. When seeds were exposed to waves with amplitude of 600 MPa, there was further delay and slowing of sprouting rate compared to the control. The sequence of the two factors had a significant effect. When seeds were first subjected to β-radiation and then shock waves, the number of sprouts that died increased by a factor of two. A decrease in the number of anomalously developing sprouts was due to the death of a number of the damaged seeds, while in the reverse sequence the seeds remained viable. A shock wave of 100 MPa slightly stimulated the sprouting of speeds, regardless of treatment sequence. Further increases in wave amplitude increased the number of seeds that did not sprout. For greater wave amplitudes the greater damage was done when β–irradiation preceded shock wave. The modal sprouting time for anomalous seeds occurred between 80 and 100 hours after they were moistened and the probability of anomalies was 45.5% when the shock wave preceded irradiation. When treatments were conducted in the reverse sequence, the modal sprouting

period for anomalous seeds was 220-240 hours and the probability of occurrence was 38.6%. These data are interpreted as suggesting that greater harm occurred in the latter case. The authors conclude that their results indirectly support the hypothesis that there is a shock wave present in the electron "envelope" of the track of heavy charged particles.

Figure 1: Dynamics of seed sprouting under exposure to β-irradiation and shock waves in different sequences

Figure 2: (1-w/z) as a function of time

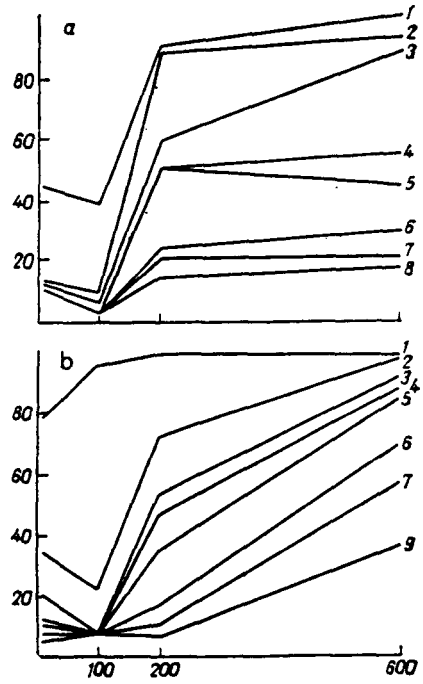

Figure 3: Relative number of sprouting seeds as a function of pressure amplitude in the front of a shock wave in the time intervals 20-40 hr (1), 41-60 hrs (2), 61-80 hrs (3), 81-100 hrs (4), 101-120 hrs (5), 161-180 hrs (6), 181-200 hrs (7), 201-220 hrs (8), 221-240 hrs (9) with shock wave first (a) or β-irradiation first (b) Abscissa - shock wave amplitude (in MPa); ordinate - seeds which failed to sprout (in %)

Figure 4: Distribution of quantity of anomalous plants across time intervals with either β-irradiation of shock wave first

CARDIOVASCULAR AND RESPIRATORY SYSTEMS

PAPERS:

P1057(23/89)* Barer AS, Breslav IS, Isayev GG, Sokol YaA.
The effects of increased respiratory resistance on human work capacity
Kosmicheskaya Biologiya i Aviaskosmicheskaya Meditsina.
23(2): 4-11; 1989.
[62 references; 36 in English]

Human Performance, Work Capacity
Humans
Cardiovascular and Respiratory Systems, Increased Respiratory Resistance

Abstract: Respiratory resistance is increased by breathing apparatus and protective respirators used mainly on high altitude flights. In general, as resistance to respiration increases, maximum physical work capacity and duration of exertion decreases. The respiratory system does not remain passive, but compensates for the new conditions: breaths become less frequent and deeper, allowing aerodynamic resistance to be overcome with less energy. This appears to be primarily a voluntary response, as it does not occur under anaesthesia. In addition, central respiratory activity increases, as shown by the increase in the so-called "occlusion" pressure or the dP/dt_{max} parameter and the electrical activity of the respiratory muscles that is based on the increased force they produce.

Increased respiratory resistance is harder to compensate for during exercise; however, adaptive restructuring of the breathing pattern does occur. Pulmonary ventilation is lower than during similar exercise combined with normal breathing conditions and does not meet the requirements generated by heightened gas exchange, potentially leading to hypercapnia and acidosis. Even light exercise and slightly increased resistance can lead to such adverse consequences if exposure continues long enough.

In endurance tests, exercise is usually self-terminated due to shortness of breath and respiratory discomfort. This effect, believed to be associated with the increased work required of inspiratory muscles, occurs much sooner if respiratory resistance is introduced. When subjects exposed to graded exercise and respiratory resistance are unable to continue due to shortness of breath, it has been found that they have reached a relatively stable maximal value for peak pressure differential in the respiratory tract. This differential is thought to reflect the "maximal cost" of adaptation. The authors conclude that the major factor limiting physical work capacity under conditions of increased respiratory resistance is the functional state of the respiratory musculature.

The authors' own research has shown that if a person is exposed to constant inspiratory-expiratory resistance and asked to perform graded exercise along with increased activity of inspiratory muscles, the phase activity of expiratory muscles gradually increases. The tired muscles cannot support the required contraction amplitude, and respiratory volume decreases. To compensate, breathing becomes more rapid, but this does not provide the needed alveolar ventilation, leading to acute hypercapnia and acidosis. Environmental hypercapnia increases this response.

It has been found that the maximal resistance that can be overcome without substantial decrease in pulmonary ventilation, is subject to great individual differences and ranges from 7.3 to 66.0 cm. $H_2O \cdot liter^{-1} \cdot sec$. Under normal respiratory conditions, people typically refuse further exercise due to exhaustion of the exercising muscles. However, under all increased resistances tested, cause for failure to continue exercise was shortness

of breath. If a coefficient K represents the ratio of work performed by the respiratory muscles to the useful work performed (e.g., on an ergometer) then the threshold for respiratory discomfort is K=0.6%. Work performed by the respiratory muscles is estimated as the mean pressure in the mouth multiplied by pulmonary ventilation. For a given individual the amount of exercise that can be performed at a given level of respiratory resistance is a function of his maximum aerobic capacity.

It is suggested that aircraft personnel who will have to perform work under conditions of heightened respiratory resistance be given preliminary training, including performance of submaximal work while using a respirator. In addition, the optimal breathing pattern for increased respiratory resistance — infrequent, deep breaths — should be taught, possibly using biofeedback.

Figure 1: Pulmonary ventilation, peak inspiratory and expiratory pressure as a function of work performed at the moment the subject cannot continue exercise while exposed to increased inspiratory-expiratory resistance

Figure 2: Changes over time in electrical activity in the respiratory muscles and respiration pattern while performing work increasing in difficulty under conditions of additional inspiratory-expiratory resistance

Figure 3: Ratio of functional respiratory reserves expended and total work capacity at the moment the subject cannot continue under conditions of inspiratory-expiratory resistance as assessed by objective parameters and subjects self-rating

Figure 4: Maximum pulmonary ventilation and corresponding work performed as a function of additional resistance

P1081(23/89) Kan YeL, Avetikyan ShT, Kan GS.
Reactions of the cardiovascular system of air traffic controllers to simulated job conditions.
Kosmicheskaya Biologiya i Aviaskosmicheskaya Meditsina.
23(2): 95 ; 1989.
[18 references]
Translation of abstract on file with the All-Union Institute of Scientific and Technical Information and the All-Union Scientific and Research Institute of Medical Information

Cardiovascular System, Blood Pressure
Humans, Air Traffic Controllers
Human Performance, Simulated Job Conditions

Abstract: Heart rate, blood pressure, systolic cardiac ejection, and an impedance plethysmogram of the head were recorded in 39 air traffic controllers before, during, and after job task performance on a training simulator. The complexity of the tasks performed during the experiment varied; and performance duration was 65-70 minutes.

It was demonstrated that task performance elicited an increase in blood pressure of 6-12% in the subjects ($p<0.001$) and the increase was proportional to the difficulty of the task being performed. The other parameters did not change significantly. After task performance terminated, diastolic blood pressure did not return to baseline for 5 minutes, showing that this parameter is relatively inert. At the same time, there was an increase in the dicrotic index of the impedance plethysmogram of the head, demonstrating increased vascular resistance in this area.

A moderate negative correlation was established between baseline value of a parameter and subsequent changes; a parameter that was relatively high at baseline increased less during work or decreased more than did one with a low baseline value. This association was most pronounced for diastolic blood pressure (BP), and least for systolic BP.

The relationships among the parameters were analyzed during performance of tasks varying in complexity. It was found that when stressful tasks were being performed, heart rate was positively correlated with BP and negatively correlated with systolic cardiac ejection. The latter association was retained after task completion, when there was also positive association between diastolic BP and the dicrotic index of the impedance plethysmogram of the head.

P1064(23/89)*Buzulina VP, Machinskiy GV, Nosova YeA, Stepantsov VI.
The effects of 30 days of hypokinesia on certain physiological and biochemical parameters during maximal exercise.
Kosmicheskaya Biologiya i Aviaskosmicheskaya Meditsina.
23(2): 40-44; 1989.
[11 references; 6 in English]

Cardiovascular and Respiratory Systems, Human Performance, Aerobic Work Capacity, Metabolism, Lactate, Pyruvate
Humans, Males
Hypokinesia with Head-Down Tilt, Exercise

Abstract: A total of 14 apparently healthy men, aged 28-35, participated in this study. Half (group A) spent 30 days under conditions of bedrest at -8° head-down tilt, while the other half (group B) performed physical exercises during the hypokinesia period. The exercise program included work with a set of bungee cords and on a special treadmill that could be "run" on in a horizontal position. The program was conducted from days 3 to 29 of bedrest on a 3-day-on, 1-day-off schedule. In each cycle, the first day concentrated on maintaining speed-power characteristics with one session utilizing 200-220 kcal. Day 2 was directed at retaining power endurance, with distance covered equal to 3700-4000 m, and energy expenditure of 230-250 kcal; day 3 concentrated on supporting general endurance and consumed 260-280 kcal. During the first stage (days 3-22) of treatment, there was one session lasting 45 minutes per day; during the second stage, (days 23-29) there were two sessions per day lasting 30 minutes each. A provocative test (involving walking until exhaustion on a treadmill at a rate of 7 km/hour with angle changing by 2.5° every 3 minutes) was administered, apparently once before and once after the bedrest period. During the test, the following parameters were evaluated: maximum consumption of oxygen ($VO_{2\ max}$, l/min), distance traversed (DT, m), total oxygen debt (OD, l) and its components. The moment anaerobic metabolism began, the so-called evoked threshold of anaerobic metabolism (ETAM) was determined using a graphic method. Peripheral blood was taken from the finger before exercise and 1-2 minutes after its completion, and the concentrations of lactate and pyruvate were measured using enzyme-spectrometric methods. The ratio of lactate to pyruvate was computed.

When the groups were tested before treatment, the majority of subjects were found to be average with respect to the functional capacity of the cardiovascular system. The two subjects who did exercise regularly were both in group A, making baseline parameters higher for this group. In group B (exercise group), the hypokinesia treatment did not induce appreciable changes in aerobic work capacity. No cardiorespiratory parameter change exceeded 3%. However, anaerobic metabolism threshold increased by 8.9% and oxygen debt by 7.7%, attributable to the "rapid (alactacid)" components of oxygen debt. The authors conclude that this group demonstrate the prophylactic measures used were quite effective. The comparable parameters for group A showed considerably lower aerobic capacity and general physical endurance. The anaerobic threshold, which increased for group B, decreased for this group. Decreased work capacity was accompanied by 24% decrease in lactate and 17.7% decrease in oxygen debt mainly due to the "slow" (lactacid) component. Because the pyruvate/lactate ratio in blood after exercise remained the same for group A subjects, the author conclude that hypokinesia's detrimental effects on physical work capacity are associated with circulatory limits (affecting blood supply to all tissues including the muscles) and decreased capacity of the cardiovascular system, rather than factors associated specifically with changes in energy supply to the exercising muscles.

Table: Change in physiological and biochemical parameters recorded in a maximum exercise test on a treadmill before and after 30 days of hypokinesia with head-down tilt.

Parameter	Group A		Group B	
	before hypokinesia	after hypokinesia	before hypokinesia	after hypokinesia
VO_2 max, l/min	3.48±0.13	3.13±0.08*	3.60±0.20	3.58±0.20
Distance traversed, m	2105±134	1682±178*	2449±258	2518±264
Oxygen debt, l:	9.06±0.87	7.46±0.37	8.83±0.72	9.52±0.75
alactacid	3.45±0.21	3.17±0.14	3.32±0.15	3.80±0.31
lactacid	5.61±0.75	4.29±0.35	5.51±0.89	5.72±0.74
ETAM, min	15.2±0.61	12.6±0.92*	16.7±2.02	18.2±2.35
Lactate, mmole/l	7.68±0.7	5.83±0.6	8.49±0.8	7.54±0.9
Pyruvate, mMole/l	0.30±0.03	0.28±0.01	0.32±0.06	0.29±0.03
Lactate/pyruvate	30±6.4	24±3.9	31±4.9	26±2.4

* difference significant, $p<0.05$

P1074(23/89)* Sinopal'nikov VI, Yegorova OV, Makarenkova IN.
Use of 24-hour EKG monitoring to diagnose cardiac arrhythmias in flight crews.
Kosmicheskaya Biologiya i Aviaskosmicheskaya Meditsina.
23(2): 80-82; 1989.
[17 references; 6 in English]

Cardiovascular and Respiratory Systems, Cardiac Arrhythmia, EKG, 24- Hour Monitoring
Humans, Flight Crew
Aviation Medicine, Diagnosis

Abstract: A total of 57 flight personnel, with mean age of 37.6 years, undergoing regular flight certification examinations served as the experimental group. A control group contained 50 males in nonflight occupations, with mean age of 35.9. No subjects showed EKG alteration or positive diagnostic indicators in tests on the bicycle ergometer.

The medical study involved consideration of medical history, including flight history, recording of resting EKG, X-rays of the organs of the chest, blood analyses, tilt test, graded bicycle ergometry, and specific tests simulating flight conditions: breathing of positive pressure oxygen, exposure to moderate hypoxia and radial acceleration $+G_z$ (only for jet pilots). In addition, a 24-hour EKG was recorded on magnetic tape and analyzed automatically. Personnel were asked to follow their normal routine of motor activity and to record all significant events with their times in a diary.

A single experimental subject complained of dropped heartbeats (heart missing a beat). This subject's resting EKG showed frequent ventricular extrasystole and he was dropped from the study. Five of the remaining subjects showed occasional monotopic extrasystoles (no more than 10 per hour) at rest. Bicycle ergometry gave rise to extrasystoles in all five subjects Four of these displayed extrasystoles in the tilt test and barochamber. In the remaining 51 subjects, no arrhythmias were noted during the tilt or barochamber tests. During ergometry one subject manifested polytonic ventricular extrasystole sufficient to stop the test. Of the eight subjects exposed to centrifugation, two cases of disrupted cardiac rhythm were observed. Thus 48 of the 56 studied revealed no abnormalities during resting EKG or in response to provocative tests. However, after 24-hour EKG monitoring arrhythmias were detected in 37 of the 56 subjects, including occasional and frequent supraventricular extrasystoles, occasional ventricular extrasystoles, periods of ventricular tachycardia, and transient atrioventricular blockade. Although transient arrhythmias may have no serious implications, extrasystoles, especially ventricular, may be associated with ischemic heart disease. In three subjects signs of coronary insufficiency were evident during ergometric exercise, while extrasystoles were noted during 24-hour EKGs leading to a diagnosis of ischemic heart disease; two other subjects showed other signs of insufficiency coupled with extrasystoles. Extrasystolic arrhythmias were noted in 64.9% of the flight crew, but only in 22.5% of the control group. The authors recommend the use of 24-hour EKGs in examination of flight crews to reveal arrhythmias, which may be the only clinical manifestation of ischemic heart disease.

Table: Nature and frequency of cardiac arrhythmias in subjects of the experimental and control groups based on data from dynamic monitoring

Figure 1: Fragment of EKG record of subject B

Figure 2: EKG fragment for subject L.

P1088(23/*89)Korkushko OV, Shatilo VB.
Orthostatic response of circulation and autonomic regulation in healthy humans varying in age.
Fiziologicheskiy Zhurnal.
35(1): 3-8; 1989.
[18 references; 8 in English]

Cardiovascular and Respiratory Systems, Circulation; Neurophysiology, Autonomic Regulation
Humans, Age Differences
Orthostatic Response

Abstract: The goal of this work was to investigate autonomic support of orthostatic reactions of the circulatory system in healthy middle-aged and elderly people. Subjects were 30 individuals in each of 3 age groups: 20-34, 60-74, and 75-80. Subjects lay supine for 20 minutes while heart rate, systolic and diastolic blood pressure were measured, and cardiac rhythm continuously registered. Cardiac stroke output was determined using tetrapolar impedance plethysmography of the chest. Cardiac output was computed from heart rate and stroke volume. Stroke and cardiac indices were calculated. Total peripheral resistance was computed from blood pressure and cardiac output. Subjects then assumed an upright position over the course of 3-5 seconds. At the end of every minute of standing, systolic and diastolic blood pressure and heart rate were recorded; the other parameters listed above were derived at minutes 1, 5, and 10. During minutes 4-5, cardiac rhythm was recorded to be used for spectral analysis. Strength of parasympathetic effects on the heart was estimated in supine and upright positions on the basis of the respiratory component of cardiac rhythm. Sympathetic effects were estimated on the basis of parameters of the Traube-Hering wave and slow cardiac rhythm waves. In addition, the percentage contribution of each component of cardiac rhythm to the entire rhythmogram was estimated. Type of blood pressure response to assumption of upright position was determined for each subject. Student's t was used to test data for statistical significance.

Upon standing up, all subjects showed an increase in heart rate and peripheral resistance, while stroke volume and cardiac output decreased. However, these parameters stabilized in the first minute for the young group, but not until minute 3-5 for the older groups. When young subjects stood, systolic blood pressure was unchanged, while diastolic pressure decreased significantly. In the middle group, systolic blood pressure decreased, while diastolic remained the same, and in the older subjects. no change occurred for the group as a whole, although individuals showed changes in different directions. All subjects displayed decreased stroke index when they stood, but this change was smaller for older subjects. On standing, young subjects displayed greater changes in peripheral vascular resistance, heart rate, and cardiac index, which the authors associate with sympathetic regulation.

In young subjects at rest, the respiratory component of the cardiac rhythm predominated, attesting to predominance of parasympathetic regulation. After they spent 5 minutes in an upright position their Traube-Hering wave increased in magnitude, and some increases were also noted in the slow component, while the respiratory rhythm decreased by a factor of three. These results suggest that the sympathetic nervous system regulates cardiovascular function during standing. In the middle age group when the subjects were at rest, all three components were reduced in magnitude indicating less autonomic tonus. The slow wave components of the cardiac rhythm were strongest, indicating sympathetic dominance. After standing, changes were analogous to those in the younger group, but the magnitude of the shifts was diminished, suggesting decreased activity of the sympathetic nervous system in the upright position. The absence of significant changes when the elderly group stood after rest indicates that sympathetic regulation of cardiovascular functioning

diminishes with age. The authors conclude that the major mechanism responsible for diminished compensatory hemodynamic response after standing is diminished sympathetic reactivity.

Table 1: Change in hemodynamic parameters when subjects varying in age assume an upright position

Table 2: Changes in hemodynamics and the periodic structure of heart rhythms as a function of type of blood pressure response to standing in subjects of varying ages

Table 3: Change in parameters of the periodic structure of cardiac rhythm upon assumption of an upright position in subjects varying in age

Figure: Changes in cardiac index, heart rate, and total peripheral vascular resistance When standing upright in young and middle-aged subjects

MONOGRAPH:

M146(23/89) Val'dman AV. Almazov VA, Tyrlin VA.
Барорецепторные Рефлексы: Барорецепторная Регуляция Кровообращения
Baroretseptornyye Refleksy: Baroretseptornaya Regulyatsiya Krovoobrashcheniya
[Baroreceptor Reflexes: Baroreceptor Regulation of Circulation;
Leningrad: Nauka: 1988.
[143 pages; 28 illustrations; 2 tables; 384 references]

Key Words: Cardiovascular and Respiratory Systems, Circulation; Neurophysiology, Baroreceptor Reflexes; Psychology, Stress, Exercise

Annotation: This book presents data on the morphological and functional structure of mechanoreceptors of the heart and large vasculature, describes neuronal and neurochemical organization of the central component of the baroreflector arch, and analyzes the mechanisms underlying hypothalamic modulation of the baroreceptor reflex.
The roles of baroreceptor reflexes in regulation of cardiac activity and vascular tonus and support of the baseline level of blood pressure are discussed. The functional significance of the baroreceptor reflex in the regulation of circulation is considered. Arguments are presented for the idea that one of the functions of the baroreflex is to support adaptive hypertension in response to aversive emotional stimuli. The authors cite their own data and that in the literature regarding changes in the baroreceptor reflex in the development of arterial hypertension.

Contents

DEVELOPMENTAL BIOLOGY

PAPERS:

P1083(23/89) Raguzin AV.
Oxygen pressure in the brain of a fetus during early stages of ontogenic development.
Kosmicheskaya Biologiya i Aviaskosmicheskaya Meditsina.
23(2): 95-96; 1989.
[31 references]
Translation of abstract on file with the All-Union Institute of Scientific and Technical Information and the All-Union Scientific and Research Institute of Medical Information

Developmental Biology, Neurophysiology, Brain Development; Reproductive Biology
Rats, Pregnant, Fetuses, Neonates
Oxygen Pressure

Abstract: In acute experiments using anesthetized (urethane 1 g/kg) rats (42) in days 19-21 of pregnancy, their fetuses (45), neonate rats (15), and nonpregnant animals (9), oxygen pressure (pO_2) was measured polarographically in the brain at various levels of oxygenation: breathing of oxygen-nitrogen mixtures (10, 21, 50% O_2) and pure oxygen. It was found that pO_2 in the brain of rat fetuses is 4.4±0.2 mm Hg, which is significantly lower than in adult subjects. Brain pO_2 of an organism developing *in utero* is virtually unaffected when the pregnant animal breathes hypo- or hyperoxic gas media, although pO_2 of the mother's arterial blood undergoes substantial changes. Brain tissue pO_2 in neonate rats was 13.0±2.1 mm Hg, which is also lower than in adult animals. When the neonates inhaled gas mixtures with elevated or depressed concentrations of oxygen, pO_2 in the brain changed accordingly, increasing in hyperoxia and decreasing in hypoxia, but returned to normal after treatment. The major feature of changes in pO_2 in the brains of neonates was the much greater maximum increase in oxygen pressure while breathing pure O— (83.1±10.2 mm Hg). When pO_2 was studied in the wall of the pregnant female's uterus, it was found that the shifts in oxygen pressure in response to hypoxic and hyperoxic breathing media were very moderate: 134.6±8.4% during inhalation of pure oxygen and 77±2.8% during inhalation of a 10% oxygen-nitrogen mixture.

Analysis of the results obtained and their comparison to data in the literature support a number of hypotheses relating to oxygen homeostasis in the developing brain when pO_2 varies in the inspired air First, pO_2 of brain tissues of fetuses and neonate rats is significantly lower than in adult animals. Second, pO_2 in the brains of fetuses is resistant to significant fluctuations in the level of oxygenation of the mother's body. At the moment of birth the development of the neonate's own mechanisms for oxygen homeostasis of the brain is not complete. The stability of pO_2 in the fetal brain is determined by mechanisms localized in the uterine-placenta region. Third, in regulating adequate supply of oxygen to the developing brain, a greater role is played by reactions protecting the brain from oxygen surfeit, than by those compensating for an oxygen deficit. On the whole, this reflects the evolution of mechanisms for maintaining oxygen balance in the brain. In early stages of phylogeny, as well as early stages of ontogeny, a low level of tissue pO_2 is normal. If at the initial stages of development of life on Earth, tissue pO_2 was low because of low atmospheric pO_2 (2-3 mm Hg), then in early ontogeny one could surmise that low tissue pO_2 is associated with the presence of mechanisms in the mother-fetus system for protecting the cerebral structures of the organism developing *in utero* from excess oxygen.

ENDOCRINOLOGY

PAPERS:

P1061(23/89)* Morukov BV, Pozharskaya LG.
Concentration of hormones regulating calcium-phosphorus metabolism in humans in reponse to 120 days of hypokinesia.
Kosmicheskaya Biologiya i Aviaskosmicheskaya Meditsina.
23(2): 26-28; 1989.
[17 references; 9 in English]

Endocrinology, PTH, STH, Calcitonin, Gastrin; Metabolism, Calcium, Phosphorus
Humans, Males
Hypokinesia With Head-Down Tilt, Long-Term

Abstract: Subjects in this experiment were 9 apparently healthy males, aged 30-42, who underwent 120 days of strict bedrest in a head-down tilt position of -4.5°. Concentrations of parathyroid hormone (PTH), somatropic hormone (STH), gastrin, and calcitonin (CT) were measured in blood serum during a baseline period and on days 8, 28, 49, 72, 92, and 112 of treatment, and on day 7 of a recovery period. Throughout the experiment the subjects consumed a controlled diet. STH and gastrin were measured using radioimmunoassay and a standard test kit, while CT and PTH were measured using a test kit manufactured in FRG. Calcium was measured titrometrically in serum, and activity of ionized calcium was registered using an ion selective electrode. Student's t was used to test results for significance.

Level of PTH was elevated throughout the treatment period and during recovery. The highest level of PTH was observed on days 49 and 112 of treatment. Calcitonin was reliably above baseline level on day 28 of bedrest only. On day 49 it was no different from baseline, and subsequently was significantly depressed. Gastrin tended to exceed baseline, but this difference was only significant on day 112 of treatment. During recovery, gastrin was significantly higher than baseline or at any time during bedrest. STH first increased on days 8-28 of treatment, then progressively decreased, dropping below detectable levels on day 112 of treatment and during recovery. Total calcium exceeded baseline starting on day 28 and continued to be high into the recovery period. Highest concentrations were noted on days 92 and 112 of treatment. Activity of the ionizing fraction was also above baseline starting on day 28 and continuing until the termination of treatment. Increased PTH is considered to be important for changes in calcium phosphorus metabolism during hypokinesia, leading to bone demineralization. Increased calcitonin and gastrin are considered a response to the higher concentrations of ionized calcium. Changes in STH are thought to be responses to increased PTH and decreased anabolic metabolism.

Table: Serum concentration of hormones regulating mineral metabolism and calcium metabolism in humans undergoing 120 days of hypokinesia with head-down tilt

P1063(23/89)* Vasil'yev VN, Lakota NG, Chekanova SL, Gudoshnikova LV.
Activity of the sympathetic-adrenal system in humans exposed to experimental simulations of weightlessness.
Kosmicheskaya Biologiya i Aviaskosmicheskaya Meditsina.
23(2): 34-40; 1989.
[10 references; none in English]

Endocrinology, Sympathetic Adrenal System, Stress; Neurophysiology, Motion Sickness
Humans, Males
Weightlessness Simulations, Suit Immersion

Abstract: This study investigated the state of the sympathetic-adrenal nervous system and other effects of exposure to "suit immersion" as a weightlessness analogue. Subjects were selected fon the basis of no paradoxical response to strong CNS stimulants and absence of respiratory anomalies. The group included 6 healthy males, aged 22-34. For 3 days, subjects wearing a special waterproof suit with an inflated collar were immersed to the neck in water at 31°. At 3 hour intervals sublingual temperature, EKG, heart rate, blood pressure, forced expiration parameters, and sensorimotor reactions to sound and light were measured. In addition, subjects responded to a questionnaire, and water consumption and diuresis were recorded. These parameters were also recorded for 1 day previous to treatment. Throughout the experiment, diet was controlled and renal excretion of adrenaline (A), noradrenaline (NA), DOPA, and dopamine (DA) were measured. . Physical work capacity was assessed before and after treatment. A fluorometric method was used for sample analysis. Data were analyzed by computer.

Heart rate, blood pressure and body temperature remained within normal limits during immersion, although in the initial treatment period heart rate was above baseline, while on day 3 body temperature had dropped somewhat. Diuresis exceeded baseline on day 1 of immersion and dropped below it on day 3. Weight loss was 2.65% of baseline. During the first few hours of treatment, subjects had difficulty breathing and showed marked hyperemia and edema of the face, with hoarseness and stuffy nose, and in some cases trouble with articulation and stomach discomfort. Some subjects complained of vestibular discomfort and headache. The second day was marked by vestibular discomfort and illusions. Some displayed signs adaptation toward the end of day 2, while in others symptoms worsened. Excretion of catecholamines showed marked effects of the treatment, involving two phases — "anticipatory," and actual stress. Over the course of the 4-day period, 6 adrenaline and 10 noradrenaline "crises" occurred, in which adrenaline or noradrenaline in urine exceeded the physiological norm by a factor of 3-5 or 2-4, respectively. All subjects manifested functional stress on the sympathetic adrenal system, but individual differences in severity were marked. Increased excretion of catecholamines was accompanied by different symptoms: adrenaline excretion was associated with listlessness, depression, headache, shortness of breath, inability to concentrate; increased noradrenaline excretion was associated with irritability, constriction of the chest, muscle pain, and vestibular symptoms; dopamine excretion was associated with muscle pain, and chest and toe constriction. In all subjects, work capacity decreased markedly after immersion. Increased sympathetic adrenal stress was correlated with large decreases in work capacity. An even stronger association was found between functional stress on the sympathetic adrenal system and severity of motion sickness symptoms during immersion. The authors consider the association between sympathetic adrenal stress, decreased work capacity, and severity of motion sickness in response to immersion to be an important result for space medicine,

Table 1: Results of analysis using the method of major components of the factor structure of experimental data on excretion of adrenalin, noradrenaline, DOPA, and dopamine in 6 subjects during baseline period and days 1, 2, and 3 of suit immersion

Table 2: Comparative assessment of functional stress on the sympathetic adrenal system with parameters of weight loss, gas and energy metabolism, and physical work capacity in 6 subjects before and after immersion, as well as motion sickness syndrome during immersion

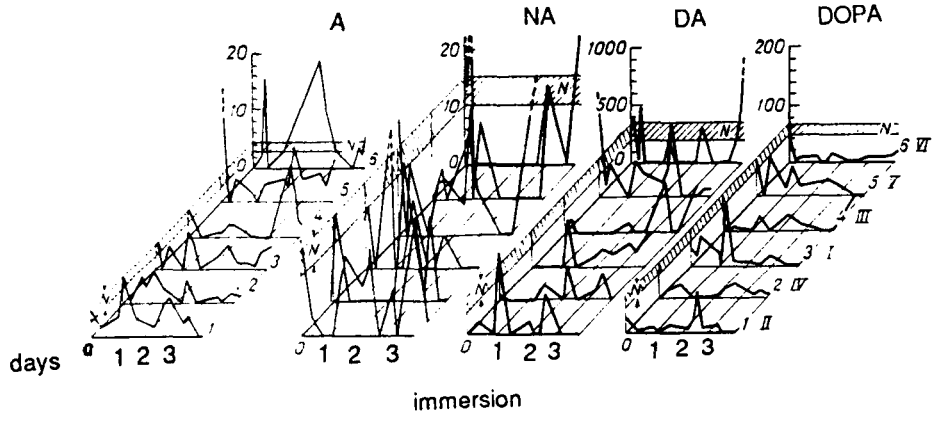

Figure 1: Changes in excretion of adrenaline, noradrenaline, dopamine and DOPA in 6 subjects exposed to suit immersion during a 4-day experimental period

Ordinate - excretion of A, NA, DA, and DOPA (in ng/min); abscissa - baseline day, days 1, 2, 3 of immersion; cross-hatched area marked with N is the range of normal values; I - IV rank of subjects on the scale of stress on the sympathetic adrenal system I = least stress.

Figure 2: Results of the analysis of the factor structure of experimental data using the chief components method

Figure 3: Changes in excretion of adrenalin, noradrenaline, dopamine, and DOPA over 4 days in subgroups having excellent and average tolerance to Coriolis acceleration

GASTROINTESTINAL SYSTEM

PAPERS:

P10666(23/89)* Andriyanko LYa, Bubeyev YuA, Gorin VV, Degtyarev VA, Kaplan MA, Remizov Yul.
The functional state of the hepatobiliary system in hypokinesia with head-down tilt.
Kosmicheskaya Biologiya i Aviaskosmicheskaya Meditsina.
23(2): 48-50; 1989.
[9 references; 3 in English]

Gastointestinal System, Hepatobiliary System, Liver, Gallbladder
Humans, Males
Hypokinesia With Head-Down Tilt, Short-Term

Abstract: In this study 16 male volunteers, mean age 29 ± 3.5 years, were exposed to hypokinesia with head-down tilt, either at -20° (n=10) for 6 hours, or at -10° for 3 days (n=6). The absorption and secretion functions of the liver, the functional state of the gallbladder and the bile ducts, and the nature of bile flow into the intestine were investigated using dynamic scintigraphy of the hepatobiliary system. These analyses required continuous recording of the progress of a intravenously administered radiopharmaceutical preparation (^{99m}Ts-HIDA) through the hepatocytes and bile ducts into the intestine. The preparation used was physiologically stable and was rapidly extracted from the blood and excreted in unchanged form, without affecting bile formation or being absorbed by the intestine or gallbladder. This preparation was transported from the blood through the hepatocyte membrane by an organic anion transmitter (the process is a function of the functional state of the hepatocytes). This treatment was performed on an empty stomach with subjects first lying in a horizontal position to produce baseline data and again at the end of the hypokinesia period. γ-radiation was measured using a γ-chamber detector parallel to the subjects' bed. In a control condition, the gallbladder was stimulated by a gall-inducing breakfast consisting of two raw egg yolks. Parameters measured included blood clearance, time of maximum accumulation of the radioindicator in the liver, and time for half the radioindicator to be excreted from the liver. Each subject's data were compared before and after exposure to hypokinesia with head-down tilt.

In baseline experiments, the gallbladder contracted spontaneously in 7 out of 16 cases without administration of the bile-producing breakfast; this was considered normal. When the bile-producing egg yolks were consumed, the gallbladder contracted in 14/16 subjects, releasing the radioindicator into the intestine. In the remaining two cases no gall bladder contraction was observed. After 6 hours of head-down tilt, no changes in liver function or bile flow were noted. In four cases, there was a significant increase in the time for half the radioindicator to be excreted from the liver, and the time for maximum accumulation of the radioindicator in the liver. Two of these four subjects had previously shown disorders of gallbladder drainage after the bile-producing breakfast, which may indirectly indicate some gastrointestinal disorder. Further examination showed these subjects to be suffering from chronic gastroduodenitis, while the other two revealed chronic [subclinical] persistent viral hepatitis. When parameters for these four subjects were averaged, maximum accumulation of the radioindicator in the liver, along with time for half the indicator to be released from the liver after 6 hours of head-down tilt, were significantly elevated for this group compared to baseline data and parameters of subjects with no sign of liver problems after head-down tilt. Subjects with no sign of dysfunction showed similar changes in parameters after a 3-day period of head-down tilt. Thus, short-term head-down tilt may be used as a diagnostic indicator of latent liver problems, while disrupted hepatobiliary

function should be considered a possible consequence of weightlessness. Those subjects with latent hepatobiliary problems.may be markedly affected by weightlessness.

Table: State of absorption-secretion function of the liver under conditions of hypokinesia with head-down tilt differing in duration

HABITABILITY AND ENVIRONMENT EFFECTS

PAPERS:

P1065(23/89)*Panferova NYe, Belakovskiy MS, Gutorova LV, Lebedev VI, Pervushin VI, Rezayeva LT, Rykova MP, Meshkov DO, Smirnov KK, Yuzhanskaya MG.
Prevention of ultraviolet deficiency during long-term human exposure to an isolated living environment.
Kosmich eskaya Biologiya i Aviakosmicheskaya Meditsina.
23(2): 59-63; 1989.
[7 references; 3 in English]

Ultraviolet Deficiency, Prevention
Humans
Habitability and Environmental Effects, Airtight Living Environment

Abstract: Two experiments were performed. In the first, 3 subjects spent 60 days in an airtight living environment with artificial illumination of approximately 70 lux. Starting on day 35 they underwent 20 UV-irradiation sessions in a dose of 0.75 MED (minimal erythemic dose). Subjects' biochemical parameters were compared post treatment with values obtained on day 11 of confinement. The second experiment was performed under laboratory conditions in the winter. One group (n=7) served as a control. Subjects in groups 2, 3, and 4 underwent 20 sessions of UV in doses of 0.75 MED (n=7), increasing doses of 0.5 to 2 MED (n=3), and increasing doses of 0.25 to 3 MED (n=3), respectively. The upper portion of the body was irradiated daily on both sides. Subjects in group 2 received 15 MED, while those in groups 3 and 4 received 30 MED. Some cases of burn were observed in group 3. MED levels, coordinates of skin color and coefficient of reflection of orange light rays were measured before, and after 10 and 20 sessions and 10 days after termination of radiation. In addition, blood was taken from the cubital vein and diurnal urine was collected. Concentrations of vitamin D and E were measured in serum, excretion of thiamine and nicotinamide was measured in urine. Mineral metabolism was assessed by measuring Ca, Mb, Zn, and Cu in serum and urine using atom-absorption and atom-emission spectrometry. Total amount of P was determined using spectrophotometry with molybdenium blue. Functional activity of lymphocytes was measured in heparinized blood, and activity of natural killers was assessed in blood.

Before and during confinement in the airtight quarters, biochemical parameters were normal. By day 35 of confinement, signs of UV-deficiency could be noted, including: decrease in MED, decrease in vitamin D in blood to the lower bounds of the norm, and pallor. After UV- irradiation in a dose of 0.75 MED, these symptoms decreased, and increases were noted in vitamins D and E in blood. Renal excretion of thiamine was also diminished. Since vitamin A is a factor in the prevention of stress disorders, its increase in blood is of direct adaptive benefit. Irradiation at this dose did not completely prevent symptoms of UV-deficiency, and not all parameters recovered to baseline. In the second experiment, vitamin levels were virtually unchanged in the control group, which received no irradiation. In all irradiation conditions, concentrations of vitamins A, E, and D in the blood increased. At various stages of the research, concentration of Ca and P in serum decreased in the control group. After 20 sessions of UV-irradiation up to 2 MED (group 3), the level of Ca and P in blood increased significantly; differences were not significant, however, for the other schedules. Renal excretion of P decreased in the control group, but remained the same in the experimental subjects. Blood and excreted Mg decreased in control and experimental subjects. Serum Cu remained the same in the control group and increased in group 2 after 10 and 20 sessions at 0.75 MED and after 20 sessions for group 3. Serum Zn increased in group 3 and for group 2 10 days after termination of irradiation. Changes in Zn and Cu were

attributed to processes of melanogenesis in skin. Subjects in group 4 showed marked changes in the amino acid spectrum of blood, suggesting dominance of catabolic processes and increased excretion of nicotinamide. One adverse consequence of UV-irradiation may be inhibition of normal killer activity. Killer cytotoxicity did not decrease in irradiated subjects and even increased significantly in group 3.

The authors conclude that UV-irradiation has a beneficial effect on humans and prevents symptoms of UV-deficiency, including increased skin sensitivity to UV-radiation and decreased metabolism of vitamins D and E. The schedule of UV-irradiation at 0.75 MED was found insufficient to compensate for prolonged confinement in an airtight environment. Dose increasing to 3 MED was found to be too strong. The authors recommend a dose of 0.75 MED for long-term use to prevent UV-deficiency. A dose increasing to 2 MED is recommended for conditions where UV-deficiency has already developed.

Table 1: Level of MED before and after UV-irradiation on various schedules

Table 2: Changes in vitamins D and E in blood in subjects in an airtight living environment before, during and after UV-irradiation in a dose of 0.75 MED

Table 3: Changes in concentration of trace elements in blood serum after UV-irradiation on various schedules

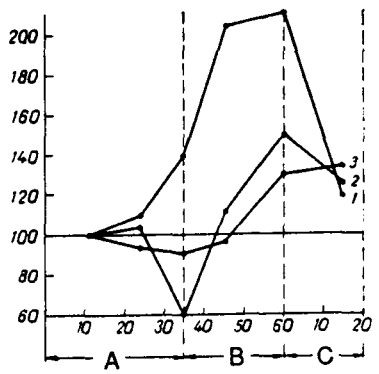

Figure Vitamin D in blood in subjects during a 60 day confinement in an airtight living environment

Abscissa - duration of confinement (in days); Ordinate - amount of Vitamin D (25 OH-D) (in % of day 11 of confinement); 1, 2, and 3 - are subject numbers; A - before irradiation, B - during irradiation, C - after leaving the environment.

P1076(23/89)* Svistunov NT, Bukharin YeA.
Reactions of the auditory, vestibular and visual systems in humans to the effects of intermittent noise.
Kosmicheskaya Biologiya i Aviaskosmicheskaya Meditsina.
23(2): 86-88 1989.
[7 references; 2 in English]

Neurophysiology, Sensory Physiology, Auditory, Visual, Vestibular Sensitivity
Humans, Operators
Habitability and Environmental Effects, Noise, Intermittent

Abstract: This work studied the effects of intermittent noise on the auditory, vestibular and visual functioning of humans. Four conditions were run on 10 apparently healthy males aged 19-22. Subjects were exposed to intermittent noise for sessions lasting 4 hours per day. The four conditions used noise levels of 95, 90, 85, and 80 dB. Each condition was run for 5 or 30 days and involved noise repeating on a 15-, 20-, or 30-second cycle, with pauses between cycles of 30 and 50 minutes. Noise stimulation was close to white noise. Background noise was maintained at a level of 75 dB. While the experiment was being conducted, subjects performed a stereotyped operator task. Physiological parameters were recorded on day 1, 5, 15, and 30 of the study before and after noise exposure, after 4 and 16 hours of rest under conditions of relative silence, and also 1, 2, 4, and 6 days after the entire set of experiments were over. Auditory sensitivity was determined through tonal audiometry on the basis of temporary threshold displacement. The functional state of the vestibular system was measured by recording head oscillations relative to the vertical axis of the body (called cephalography). Visual status was assessed using critical flicker fusion frequency (CFFF).

All three systems studied were found to be affected by intensity and duration of noise stimulation. For example, after 5 days of exposure to noise of 90 dB, threshold of sensitivity to a sound frequency of 4000 Hz was displaced by 19 dB; for exposure to noise at 95 dBa displacement was 24 dB. In both cases normal threshold was restored after 2 days. When duration of noise was increased auditory threshold displacement also increased. On day 15 of exposure displacement was 75-80% of its maximum value. Normal auditory threshold did not recover until 6 days after the 15-day exposure to noise of 80 and 85 dB. Vestibular balance function also depended on intensity and duration of noise exposure: 16 hours were required for recovery of normal balance after 5 days of exposure to noise of 95 and 90 dB, and 2 days for recovery after 30 days of exposure. Lack of dizziness in subjects suggests that effects on the vestibular system were functional in nature. Decrease in CFFF occurred after as little as 30 minutes of exposure to noise. CFFF decrement (12%) was the same after 5 days and 15 days. A 16-hour rest after 5, 15 and 30 days of exposure to noise produced only a partial CFFF recovery.

The authors conclude that short-term (4 hours per day for 5 days) exposure to intermittent noise at 90 and 95 dB leads to functional changes in the auditory, vestibular, and visual systems and is unacceptable for human operators. Long-term (30 days for 4-hours per day) exposure to intermittent noise equivalent to 80 and 85 dB, which is characteristic of certain workplaces, also leads to marked changes in sensory functions, possibly as harmful as shorter exposure to higher levels of noise.

P1060(23/89)* Berlin AA.
Development of a regimen for sanitary-hygienic procedures (i.e., a washing regimen).
Kosmicheskaya Biologiya i Aviaskosmicheskaya Meditsina.
23(2): 21-26; 1989.
[17 references; 1 in English]

Hygiene, Skin Parameters
Humans, Male and Female
Habitability and Environmental Effects, Showering Schedule

Abstract: This study was intended to investigate whether frequent washing is really beneficial and to determine an optimal washing regimen of washing in space. In different conditions, 14-19 apparently healthy individuals of both sexes, aged 25 to 45, were subjects Distilled water without additional cleansing agent was used for washing and then analyzed for chemical and microbial status. Subjects wore protective clothing to minimize exogenous contamination. Subjects washed in a specially constructed stall with 10 l of distilled water at a temperature of 42±2°C at a flow rate of 1 l/min. Water was collected from the floor of the stall. Intervals between washing were 1, 2, 3, and 4 days. The time required for wash water oxidation (chemical composition of wash water) to stabilize was measured. . Along with oxidizability, wash water was analyzed for: conductivity, chlorides, hardness, pH, odor, color, transparency, and total number of microorganisms. Subjects put on fresh clean clothing after each washing, and the stall was sterilized between showers. Before and after showering, subjects body temperature, blood pressure, heart rate, and skin pH and eH were determined. Only subjects with these parameters within normal limits were allowed to participate in the study. Atmospheric parameters were held constant. Before the beginning of the study, subjects washed carefully with their own cleansing agents and then with distilled water to remove traces of the cleansers. Then they took their first experimental shower. No washing was permitted between showers.

It was determined that maximum level of endogenous pollution occurs 3-4 days after a shower and then remains stable for a long period with clothing changed once every 7-10 days After the skin has been thoroughly cleaned, oils are completely restored in 3-4 hours. Subsequently secretions from oil and perspiration glands cease. However, maximal skin contamination does not occur 4 hours subsequent to washing, but between 1 and 3 days afterwards. Results of the study indicated that wash water contains a significant amount of desquamated epidermis. To better study this process, the epidermis was stained green and the shedding of skin in wash water studied under conditions of regular washing without cleansing agents. It was found that, with the exception of skin on the calves, washing with water virtually doubled desquamation of the epidermis. Exact rate of increase depended on whether skin was dry, oily, or normal. However, when wash water composition (averaged over 4 days) was compared for subjects with dry, oily, and normal skin, it was found that parameters were virtually the same. The author believes that for dry skin types the main burden of stabilizing skin microflora is borne by desquamation, while for oily skin, similar homeostasis is achieved primarily through the bactericidal properties of skin oils. People with dry skin lose more epidermis when they shower than those with oily skins, because skin oils provide a protective layer. When the amount of perspiration, as measured by electroconductivity and salt content of wash water, was compared for subjects with different skin types, it was also found to be virtually identical. Skin microflora was also comparable for all skin types.. The author concludes that the optimal showering frequency is once very 4 days, to allow natural homeostatic mechanisms to operate.

Table 1: Physical-chemical and microbial parameters of wash water as a function of skin type and time since washing

MONOGRAPH:

M145(23/89) Kogan AB, Vladimirskiy BM.
Функциональное Состояние Человека Оператора: Оценка и Прогноз
Funktsional'noye Sostoyaniye Cheloveka Operatora: Otsenka i Prognoz. ***[Functional State of the Human Operator: Evaluation and Prediction;.***
No 58 in Series: Problemy Kosmicheskoy Biologii; Проблемы Космической Биологии [Problems of Space Biology]
Leningrad: Nauka; 1988.
[212 pages; 38 Figures; 28 tables; 322 references]
Authors' Affiliation: Neurokinetic Research Institute, Rostov University

KEY WORDS: Human Performance, Psychology, Neurophysiology, Functional State, EEG Dynamics, Man-Machine Systems, Mathematical Modeling

Annotation: This monograph considers a broad range of theoretical and applied issues associated with the study of the spatial and temporal organization of the electrical activity of the brain of a human operator. It discusses new mathematical methods for analyzing EEG activity for diagnosis and prediction of functional state. The authors propose a number of integrated criteria which make it possible to plan ways to correct functional state. They consider the possibility that models of cause and effect relationships can be used to predict EEG dynamics. They discuss future prospects for using the methods proposed to improve complex man-machine systems and increase their reliability.

CONTENTS

M147(23/89) Dikaya LG, Zankovskiy AN, Sukhodoyev VV, Mitrofanov BN (editors).
Функциональные Состояния и Эффективность Деятельност Человека-Оператора в Режиме Непрерывной Деятельности
Funktsional'nyye Sostoyaniya i Effektivnost; Deyatel;nost Cheloveka-Operatora v Rezhime Neprerivnoy Deyatel'nosti
[The Functional State and Performance Efficiency of a Human Operator On a Uninterrupted Work Schedule [Sleep Deprivation;]
Moscow: Institute of Psychology, USSR Academy of Sciences; 1977
[291 pages]

KEY WORDS: Human Performance, Functional State, Human Operator, Sleep Deprivation, Psychology, Extreme Conditions, Group Dynamics, Adaptation

Annotation: This collection is devoted to problems in simulating and studying the functional state and performance of a human operator under extreme conditions. It is demonstrated that the experimental model of an uninterrupted work schedule is a method for simulating and performing systems analysis of human performance under extreme conditions, which allows a comprehensive investigation of the psychological and psychophysical mechanisms underlying regulation of performance and state, and identification of the temporal pattern of changes in operator performance efficiency.

The book contains analyses and interpretations of results obtained in laboratory and field studies, and a discussion of future prospects for studying the problem.

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SECTION 2. DIAGNOSIS AND CONTROL OF THE FUNCTIONAL STATE OF A HUMAN OPERATOR

IMMUNOLOGY

MONOGRAPH:

P148(23/89) Konstantinova IB.
Sistema Immuniteta v Ekstremal'nykh Usloviyakh: Kosmicheskaya Immunologiya. Система Иммунитета в Екстремальных УсловияхЬ Космическая Иммунология [***The Immune System Under Extreme Conditions:: Space Immunology***] No. 59 in the series Problemy Kosmicheskoy Biologii. Проблемы Космической Биологии. [Problems of Space Biology]. Moscow: Nauka; 1988.
[289 pages; 11 Tables; 42 Figures; 688 references]

Annotation: This monograph summarizes and analyzes results of the study of the human immune system under exposure to extreme conditions (hypokinesia, experimentally induced stress, airtight living quarters, space flight). Adaptation to extreme factors were studied using modern immunological, immunochemical and radiological methods. The results of research performed in weightlessness on isolated human lymphocytes and of experiments performed on animals on COSMOS biosatellites are cited. The prospects for future development of space immunology are discussed in connection with general problems of space medicine and the practice of public health, as well as the extensive opportunities for using the results obtained in clinical practice. This monograph is intended for immunologists, biologists and medical personnel (including stomatologists).

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LIFE SUPPORT SYSTEMS

Special Feature: ***Life Support Systems: Biomedical Support of Manned Flights to Mars***

By. Gazenko OG, Grigor'yev AI, Il'yin YeA, Institute of Biomedical Problems; USSR Ministry of Health

In: Zemlya i Vselennaya; 1988 (5): 15-20.

KEY WORDS: Operational Medicine, Biomedical Support, Space Flight, Manned, Mars, Life Support Systems, CELSS, Habitability and Environmental Effects, Psychology, Radiobiology, Metabolism, Musculoskeletal System, Immunology, Gravitational Biology, Artificial Gravity

Text: Soviet space medicine and biology has attained outstanding results in supporting long-term space flights. The experience that has been acquired in this area provides a good basis for a manned expedition to Mars, and General Secretary M.S. Gorbachev has proposed to U.S. President Reagan that Americans participate in this endeavor.

Flight to other planets is one of our most enthralling problems and one which has long attracted the attention of humanity. But much of what has seemed impossible for centuries, and which only yesterday was still a dream, is swiftly becoming reality. The history of the development of cosmonautics confirms the accuracy of the words of our great countryman, K. E. Tsiolkovskiy: "What is impossible today becomes possible tomorrow."

And today's plans for a manned flight to Mars, which may also seem fantastic at times, have a very real basis. First and foremost, this basis includes the enormous successes in scientific and technological progress on the whole and cosmonautics in particular. All that was accomplished on manned long-term space flights, where the priority of Soviet science is firmly established, the outstanding functioning of the space technology, the health of the cosmonauts during these flights and after their return, without question, instil optimism concerning even longer human sojourns in space and the prospects of successfully surmounting the physiological barriers weightlessness.

Today the range of opinions concerning the possible timetable for implementing the Mars flight is rather broad, ranging from the most optimistic estimates of a manned flight before the end of this century, to the very cautious, and thus more remote timeline. All this is highly natural. After all, prediction is a very complicated process. One thing is beyond doubt -- this will be but a single step into the unknown. And each such step must be based on knowledge that has already been acquired, evaluation of all previous experience, a balanced analysis of actual conditions and possibilities. This is particularly true with respect to the health and safety of human beings. It was precisely this sort of approach that allowed Yu. Gagarin to blaze the trail into space, A. Leonov to perform an EVA, and N. Armstrong to walk on the moon.

Of course, the experience with biomedical support of man in space acquired in previous years provides a good start for the future in space. However, a great deal more needs to be done if we are to fully solve the problem of a manned Mars flight.

One of the chief and unavoidable biomedical problems of a Mars expedition is the issue of habitability, i.e., the biological sufficiency of the living environment in the spacecraft, and its appropriateness to the long-term biological needs of humans. This aspect of habitability has not yet become the object of scientific analysis, much less of experimental research, although certain initial ideas were expressed as early as the 1970's. It is intuitively

obvious to physicians and biologists that we will have to confront this problem when man is separated from the Earth for long periods of time. This follows logically from the fundamental principle of natural science concerning the unity of organism and environment. Of course, this refers to the natural environment in the Earth's biosphere, in which man's long-term natural needs developed during the long process of human evolution. From the standpoint of space medicine and ecology, it is precisely this biosphere that is the standard for the human living environment, and the longer man is to be separated from conditions on Earth, the closer the actual artificial living environment on the spacecraft must be to this standard. Such an approach is essential in planning a manned space flight to Mars.

Before now, the ecological concept of the cosmonaut's living environment was rarely used in the actual medical support of space flights. Instead, the concept of life support systems (LSS) was used, with its associated "quartermaster's" logic: an LSS must provide man with oxygen, water, food, and remove carbon dioxide, etc. But in connection with the prospects for interplanetary cosmonautics, we can no longer speak of "provision" or "supply." but of an all-encompassing, biologically sufficient living environment for man, one that approaches terrestrial standards.

Thus, the transition from flights in Earth orbit to interplanetary flights and planetary bases requires a completely new approach to understanding the conditions for long-term human existence in an artificially created environment, along with the development of a theory of a living environment on a broader ecological scale. Probably, such new thinking will turn out to be one of the most important tasks of space hygiene and human ecology. But this is a task for the science of the future.

With regard to a Mars flight, the first step is to provide a sufficient living environment for man that will be available in the near future. There is only one way to create a functional analog of the natural environment away from the Earth -- and that is to make use of natural biological processes, arising from the interactions of plants, animals, microorganisms, and to develop a natural environment based on terrestrial biology. This goal may be attained by creating ecological systems that are closed from the standpoint of substances, within which man functions as one of the essential functional components. Biologically sufficient living environments for humans in such systems will form by virtue of the same biological mechanisms that exist in nature, independent of the defects in our current knowledge both of the mechanisms themselves and of the biogenic components of the natural environment.

By now we have created and studied various laboratory models of systems that include man and are based on the functioning of one-celled algae, higher plants, and microorganisms. These provide not only for the regeneration of the atmosphere and water, but also some vegetable nutrients. In such models, 80-90% of the substances consumed by man are generated within the system. In addition, the use of certain animals to produce a portion of the animal nutrients is being studied.

For flights to Mars, it would hardly be expedient to propose a full-scale biological system, capable of meeting all human needs. For flights of this duration there is no need for such a system and it would scarcely be profitable, since it would weigh a great deal and require a large expenditure of energy.

However, neither it would it be desirable to propose a physical/chemical system of regeneration, even though the separate technologies for obtaining oxygen and water from human waste products have been developed. At the present time, such a system would be the most efficient in terms of weight, size, and energy requirements; however, such a system cannot create a biologically adequate living environment for man, which is crucial given the relatively long duration of a Mars flight.

In our view, the most promising would be a combined system, that includes both physical/chemical and biological processes. The presence in an LSS of photosynthesizing organisms and selected animals will make it possible to partially reproduce natural plant and animal foods, and also to move the human living environment closer to natural conditions, i.e., make it more adequate in the biological sense. To achieve this, the area required by the major biological components within the overall LSS complex will be rather large, although undoubtedly limited by the weight, volume, and energy constraints of the manned spacecraft. At any rate, if the biological LSS is to play an appreciable role in the formation of a biogenic environment, the efficiency of the photosynthetic processes in regenerating the atmosphere must be no less than 30-40% nominal. Of course, this is only a preliminary estimate, requiring experimental confirmation.

The proposed biological system may be represented by one-celled algae, higher plants, and certain animals, for example, domestic birds or fish. Apart from its contribution to the regeneration of the spacecraft's atmosphere, such a system would perform certain additional functions to optimize the environment: purifying the atmosphere from water-soluble volatile contaminants; stabilizing the number and species composition of microflora in the spacecraft through antagonistic microflora; optimizing the aero-ion composition of the atmosphere; limiting the dust and heavy aerosol particles in the atmosphere.

The inclusion of a biological system in the overall LSS complex will help answer certain questions arising in connection with the possible consequences of long-term exposure of humans to a totally artificial, abiogenic living environment.

The most important feature of man's flight to Mars, from the standpoint of radiation safety, involves the absence of the shielding effect of the Earth's geomagnetic field. On flights in Earth orbit, this field decreases the dose of galactic and solar cosmic radiation, and, as long as the space flights, remain below the Earth's radiation belts, serious problems do not arise. However, on interplanetary flights, galactic cosmic radiation, which consists of nuclei of chemical elements moving at relativistic velocities, become significant.

On the basis of certain experiments, researchers propose that during a 2-year sojourn in space, one may expect the loss of a relatively small number of nerve cells in the human cerebral cortex, due to the effects of relativistic nuclei of atoms. At any rate, losses should remain within limits comparable to losses through natural aging. However, from the biological point of view, the topography of the tracks of heavy particles is important, especially where they pass through clusters of nerve cells composing a vital nerve center of the brain. Thus the future of interplanetary flight depends largely on the solution of this problem.

Since the dose of galactic cosmic radiation is a function of phase of the solar activity cycle, and protection from such radiation (using shielding of reasonable thickness) is ineffective, it would seem desirable to conduct flights during periods of maximum solar activity, which correspond to minimal galactic cosmic radiation. At such periods the frequency of phosphenes, induced by particles of galactic cosmic radiation, in the eyes of the cosmonauts is also at a minimum.

In order to reduce radiation danger from solar flares (their frequency is maximal during period of maximal solar activity) to acceptable levels, it is essential that space stations contain a radiation shelter that can provide reliable protection against solar cosmic rays while not exceeding weight standards, as well as an autonomous, highly reliable system for monitoring radiation and predicting danger that will give cosmonauts with enough time to take shelter in this structure. The methods to be used in such a system and its design

present a scientific and technological problem. However, it will be a great deal easier to solve than the problem of providing protection from galactic cosmic radiation.

Effective means of providing radiation safety on a flight to Mars may include pharmacological prophylaxis, strict measurement and regulation of radiation dose absorbed by each crewmember, diagnosis of the state of the cosmonauts using appropriate examination systems by a cosmonaut-physician, and, finally, use of supplementary local shielding where required.

Despite existing controversies, specialists agree that the present level of technology bodes well for a positive solution to the problem of providing radiation safety on flights to Mars.

Crewmembers must be prepared psychologically to undertake a flight to Mars, which is unavoidably associated with a certain degree of risk. Of course, past experience, together with further determination of the circumstances that man may encounter on the flight to Mars, will have great significance here. For this reason, the preparatory stages for this flight are important: first unmanned flight to Mars; then landing on the planet; return to Earth, etc. An extremely important aspect is the creation of absolute faith in the technology used to implement the flight, and confidence that all its systems are failsafe and that the crew can perform any repairs necessary.

Undoubtedly, the size of the crew will be determined mainly by design features of the technical systems and the program of scientific work to be performed during the flight and on the surface of Mars. In the opinion of the psychologists, the crew should consist of all males and must not exceed 6-8 men. The crew must consist of mature people, aged 35-45, specialists having experience in their profession and life. An obligatory qualification is past experience with space flight. It is not essential that these flights be comparable in duration with the Mars flight, but it is desirable that crewmembers have had experiences with flight at least 6 months in duration, which would allow them to grow accustomed to life in a spacecraft with all its unique features. It is essential that one crewmember be a highly qualified physician with good training in the areas of therapy, surgery, psychotherapy and psychology.

The manned flight to Mars will require the solution to problems associated with a number of physiological effects occurring in response to long-term exposure to weightlessness. In the past, space medicine has acquired considerable understanding of the effects of weightlessness on human physiology. More than 300 individuals have completed space flights varying in duration. Five Soviet cosmonauts have spent more than 300 consecutive days in space, and Yuriy Romanenko has spent a total of 430 days in space. On previous flights, much attention was devoted to medical studies and experiments, and thus one can say that a good foundation has been laid for further advances along the road to space.

Today we know a great deal about the reactions of the organism to weightlessness, and generally understand the mechanisms through which they arise. It has been established in particular that man is capable of satisfactorily adapting to long-term exposure to weightlessness, and, when long term flights are over, readapt to the Earth's gravity. We comprehend the general course of the process of adaptation to weightlessness, the phases of this process, and the state of various physiological systems which are involved during one or another stage of adaptation.

The creation by Soviet scientists of systems for preventing the adverse physiological effects of weightlessness have allowed cosmonauts, even on the longest flights, to withstand weightlessness relatively successfully and has prepared them for their return to Earth's

gravity. Of course, there is still room for improving the prophylactic system and work is continuing in this direction.

Let us briefly list the changes in the organism that should be focussed on in relation to future manned flights to Mars. First, there are changes in musculoskeletal system. Until now, even on the longest duration flights, we have fortunately not observed substantial changes in the musculoskeletal system. Moreover, through adherence to a rational approach to the use of a set of prophylactic measures, these changes in some cosmonauts were less severe after long-term flights than had previously been found after short-term ones.

Long-term exposure to weightlessness induces certain changes in metabolic processes. In particular, decalcification occurs, i.e., there is a loss of calcium, mainly in the skeleton. Until now, we have coped successfully with this by using prophylactic measures, but it should not be forgotten that these flights were of considerably shorter duration than the future flight to Mars. Changes in immunological reactivity have also been noted on long-term flights; in the absence of effective prophylactic measures the likelihood of disease occurring is increased. Reactions of the blood system to weightlessness are also not completely understood.

Now, let us say a few words about artificial gravity as a prophylactic measure. In one of the meetings of the Moscow International Forum, devoted to the 30th anniversary of the space era, cosmonauts and astronauts spoke in favor of a flight to Mars in weightlessness without centrifuges. The medical personnel were for the creation of artificial gravity on board the spacecraft. Science must accumulate the results necessary to provide a a well-thought-out answer. For the time being, persuasive data supporting one or another solution do not exist.

On the whole, the further accumulation of medical and biological information must lead us not only to a more thorough evaluation of the role of man in space, but also to a more complete understanding of the possible complications and difficulties which he might encounter on future flights. In essence this will entail continual improvements in the safety of flights through increases in the reliability of space technology, as well as the reliability of man himself.

This article, of course, does not cover the entire range of problems associated with biomedical support of a manned flight to Mars. This is only an attempt, from the standpoint of the knowledge at our disposal today to describe some of the major problems which will have to be solved on the road to further exploration of space. Unquestionably, as knowledge is acquired, our ideas about these problems and the prospects for solving them will change.

We should also expect the unexpected. Such is the logic of scientific exploration -- one advances on the basis of results obtained earlier, and encounters new and (as a rule) more complex problems.

Today, when humanity stands on the threshold of the 21st century, we can observe the ancient and eternally youthful goal of conquering space. Humanity has embarked on the road to the stars and their is no end to its advance. Flight to Mars is a very complex problem. It will require enormous expenditures, along with the development and assimilation of the most complex technology. The uniting of peoples' efforts in the name of peaceful exploration of space is a worthy goal which justifies enormous efforts to send this flight to Mars.

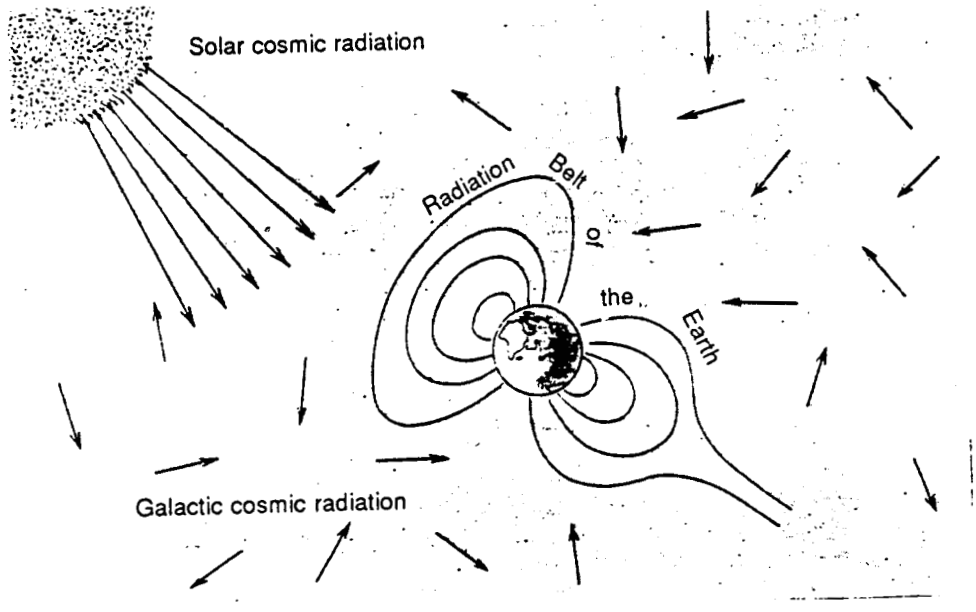

Figure 1: Sources of radiation danger in space

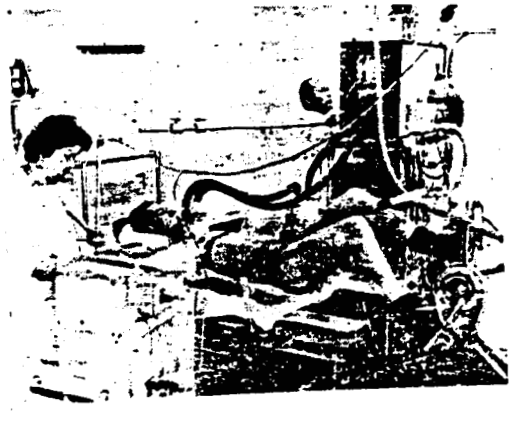

Figure 2: Research on the cardiovascular and respiratory systems of humans during physical exercise on a bicycle ergometer.

Centrifuge for creating artificial gravity on the COSMOS-936 biosatellite (1979). Postflight examination showed that to some extent artificial gravity prevented adverse physiological changes induced by weightlessness in the animals.

MAN-MACHINE SYSTEMS

MONOGRAPH:

M148(23/89) Zalikhanova NG (editor).
Бионика и Биомедкибернетика-85: Материалы Всесоюзной Конференции Биотехнические Системы
Bionika i Biomedkibernetika-85: Materialy Vsesoyuznoy Konferentsii: Biotekhnicheskiye Sistemy
[Bionics and Biomedical Cybernetics-85: Material (paper abstracts) from an All-Union Conference: Biotechnical Systems;]
Leningrad: USSR Academy os Sciences. Scientific Council on the Multidisciplinary Problem of Cybernetics; 1986

KEY WORDS: Man-Machine Systems, Bionics, Operational Medicine, Biomedical Cybernetics, Human Performance, Mathematical Modeling, Psychology, Stress, Self-Regulation, Equipment and Instrumentation, Cardiovascular and Respiratory Systems, Neurophysiology, Biological Rhythms

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MATHEMATICAL MODELING

PAPER:

P1075(23/89)*Maknenko AA, Popov VI, Sergeyev ST.
Use of cluster analysis in biomedical investigations of a man-environment system using small samples.
Kosmicheskaya Biologiya i Aviaskosmicheskaya Meditsina.
23(2): 83-86; 1989.
[10 references; 2 in English]

Mathematical Modeling, Cluster Analysis, Biomedical Data, Small Sample, Metabolism
Humans
Habitability and Environmental Effects, Airtight Environment

Abstract: This paper discusses several methodological aspects of the statistical processing of biomedical data obtained in a long-term study using a small sample. The study involved 8 healthy subjects performing operator tasks in an airtight environment with regulated microclimate. On 12 occasions, blood and urine were taken from each subject and a total of 89 parameters indicative of various aspects of metabolism and organ functions were determined. The BMDP (biomedical data program) statistical package was used to process data. Parameters were tested for significant differences using Student's t and analysis of variance. In addition, an algorithm for cluster analysis of the variables, based on minimal local and mean distance, was used.

Comparison of alternative statistical analysis methods used to evaluate these data, revealed that certain parameters indicative of various types of metabolism responded identically to environmental factors; for example, alkaline phosphatase of blood serum, organic acids in urine, and Na/K ratio in urine. Such information could not be obtained with the other statistics used. The authers recommend cluster analysis for enhancing the potential interpretation of data obtained from small samples.

Table 1: Differences from baseline of 11 sets of biochemical parameters using different statistical analysis procedures

Table 2: Congruence of response of independent metabolic parameters as revealed by the results of cluster analysis

PAPER:

P1062(23/89) Zezerov AYe, Ivanova SM , Morukov BV, Ushakov AS,
Lipid peroxidation in the blood of humans undergoing 120 days of hypokinesia with head-down tilt.
Kosmicheskaya Biologiya i Aviaskosmicheskaya Meditsina.
23(2): 28-33; 1989.
[30 references; 9 in English]

Metabolism, Lipid Peroxidation, Mineral Metabolism
Humans
Hypokinesia With Head-Down Tilt, Long-Term; Countermeasures, Nutrition, Vitamin E, Amino Acids, Folicobalamine; Exercise

Abstract: A total of 11 people were studied during a baseline period, while undergoing 120 days of hypokinesia with head-down tilt (-4.5°) and on days 7 and 25 of recovery. Subjects were divided into three groups. Group 1 (3 people) was the control. Group 2 (n=4) received vitamin E (5% oil solution of alpha-tocopherol acetate) and a regulator of calcium metabolism xydiphon (2% water solution) daily throughout treatment. Starting on day 72 they also received a preparation containing lipotropic (vitamin F-99 - a mixture of linoleic and linolenic unsaturated fatty acids in a ratio of 1:1) and hemostimulating (folicobalamine) agents, and also an agent (glucomac) preventing the disruption of mineral metabolism and having an antihypoxic effect. Group 3 (n=4) performed graded physical exercise and passive extension of antigravity muscles on a schedule of 3 days exercise, 1 day off. Lipids were isolated from venous blood and the concentration of endogenous products of lipid peroxidation (hydroperoxide and end products of their decomposition) was determined using a method not described.

Activity of superoxide dismutase was measured in erythrocytes by a method not described using a phenazine methosulfate — NADH system as a source of superoxide radicals. The unit of enzyme activity selected was 50% inhibition of the rate at which recovery to tetranitrosol blue in formazan occurred, and was computed for a milligram of hemoglobin per minute. Erythrocyte catalase activity was estimated on the basis of decomposition of exogenous hydrogen peroxide at a wavelength of 240 nm and was expressed in micromoles of hydrogen peroxide per milligram hemoglobin per minute. Concentration of hemoglobin in erythrocytes was estimated using cyanmethemoglobin.

Throughout the treatment period, concentration of blood lipid peroxides was elevated in the control group, with effects most pronounced during days 28-72 of hypokinesia. During the recovery period this parameter normalized, but end products of lipid peroxidation remained elevated. In two out of the three control subjects, activity of superoxide dismutase decreased during the treatment period and increased during recovery, while catalase activity in the erythrocytes of these subjects increased significantly and was correlated with the accumulation of hydroperoxides and lipid peroxidation end products. The third subject tended to have elevated superoxidedismutase activity with catalase activity virtually unchanged.

Group 2, the members of which received supplementary vitamins and other drugs, displayed less marked activation of the process of free-radical lipid peroxidation in blood, and never exceeded the physiological norms. On day 7 of recovery, level of lipid peroxidation end products was significantly below baseline and on day 25 had returned to normal. Individual differences were less marked in this group than in the control. The authors associate the effects of the pharmacological treatments with the antioxidant effects of vitamin E, while the

drugs used may have acted to normalize calcium and lipid metabolism. Subjects in group 3, the exercise group, showed less evidence of increased products of lipid peroxidation than the control group; no marked individual differences were revealed. As was the case with the drug group, normalizing effects were more marked when end products of lipid peroxidation were measured and less so when primary products (hydroperoxide) were assessed. The effect of exercise was somewhat less than that of the drugs. Both drugs and exercise are recommended as prophylactic countermeasures to increase tolerance of the effects of extreme factors on lipid metabolism.

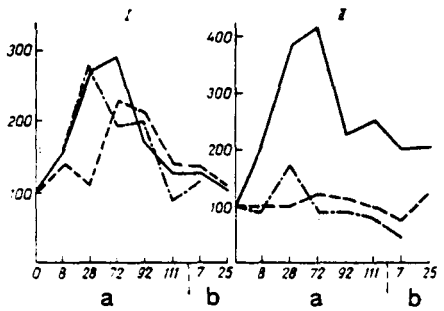


Figure 1: Lipid peroxidation in the blood of different groups of subjects exposed to 120 days of hypokinesia.

A - hypokinesia; B - recovery period. Abscissa — time (in days); ordinate — I - lipid hydroperoxides; II — end-products of lipid peroxidation (in % of baseline, mean values). Solid line — control group; dotted line — "pharmacological" group; dots and dashes — "exercise" group.

Figure 2: Changes in activity of superoxide dismutases in erythrocytes in response to 120 days of hypokinesia

Figure 3: Changes in activity of catalases in erythrocytes of control subjects.

P1078(23/89)* Shatemirova KK, Min'ko YuV, Zelenshchikova VA.
The effects of adaptation to barochamber hypoxia on certain parameters of biogenic amine metabolism in rats.
Kosmicheskaya Biologiya i Aviaskosmicheskaya Meditsina.
23(2): 89-91; 1989.
[7 references; 3 in English]

Metabolism, Biogenic Amines
Rats
Adaptation, High Altitudes, Barochamber

Abstract: An experiment was performed on 170 white outbred male rats, 30 of which animals were adapted to acute barochamber hypoxia through 6 hours of exposure to an altitude equivalent of 6500 m. Adaptation to chronic hypoxia was created by "raising" 100 animals to 6500 m for 6 hours daily for 40 days. Barochamber "ascent" started with 1500 m and was increased by 1000 m daily. Animals were sacrificed through decapitation after 5, 14, 21, 30, and 40 days of adaptation. A control group was not exposed to hypoxia. Mitochondrial membranes were isolated from the liver, brain, heart, and kidneys and activity of monoamine oxidases was measured through liberation of ammonia. In the same tissues and also the adrenal glands, the concentration of amines and their precursors (adrenaline, noradrenaline, DOPA, and dopamine) were measured fluorometrically. Concentration of protein was measured using Lowry's method. Results were statistically tested against the t criterion and revealed a decrease in total activity of types A and B monoamine oxidases (MAO) in all the tissue studied in rats exposed to both acute and chronic hypoxia. After 5 days of hypoxia, there was a sharp decrease in enzyme activity, which normalized somewhat by day 21 without attaining baseline levels. Subsequent to this (days 30 and 40) activity decreased. Type A MAO, which is a substrate of serotonin, was more sensitive to hypoxia than type B. Level of biogenic amines after one-time exposure to acute hypoxia increased in all organs studied, especially in the adrenal gland. The effect of chronic hypoxia involved an increase followed by a decrease to control values or below. The rapid response of MAO suggests the possibility of its participation in adaptation to oxygen insufficiency. During later periods (days 30 and 40), MAO activity was considerably lower than expected, suggesting that these biochemical changes are the basis of adaptive reactions. Evidently, during early stages of adaptation to hypoxia, there is an intensification of sympathetic effects accompanied by a decrease in activity of amino oxidase and some increase in levels of biogenic amines. However, when adaptation occurs at a molecular level, these physiological responses diminish.

Table 1: Activity of MAO in various tissues of rats adapted to acute barochamber hypoxia

Table 2: Concentrations of biogenic amines in various tissues of rats adapted to acute barochamber hypoxia

Figure 1: Activity of MAO in the liver, brain, heart and kidneys of rats adapted to barochamber hypoxia varying in duration

Figure 2: Concentration of biogenic amines in the liver, brain, heart, kidneys, and adrenal glands of rats adapting to barochamber hypoxia varying in duration

MICROBIOLOGY

PAPERS:

P1073(23/89)* Drugova NA, Chernova LS.
A comparative ecological study of the microbial cenosis of the lettuce rhizosphere under different conditions of cultivation.
Kosmicheskaya Biologiya i Aviaskosmicheskaya Meditsina.
23(2): 75-79; 1989.
[17 references; 6 in English]

Ecology, Microbial Cenosis
Microbiology; Botany, Higher Plants, Lettuce Rhizosphere
Cultivation Conditions, Space Greenhouses

Abstract: The goal of this study was to investigate the growth of microorganisms on higher plants cultivated under conditions similar to those projected for "space greenhouses." Lettuce plants were cultivated in airtight and open cultivation devices consisting of two containers. The upper one contained "balkaniya," a natural mineral-rich zeolite, consisting of granules of various sizes, while the lower one contained distilled water. The balkaniya substrate was moistened by capillary saturation. Plants were grown under the following conditions: illumination of 45-50 W/m^2; air temperature 21±1°C, relative humidity 65±5%, air flow rate 0.5 m/sec. The following conditions were run: 1) plants watered with distilled water; 2) the same with the addition of humates (2 g per 1 kg substrate); 3) watering with preserved water containing up to 0.5 mg silver per liter of water; 4) watering with preserved water with the silver ions removed; 5) 12- 16 hours light period on a substrate with granules 1-3 and 3-5 mm in size. The humates were obtained using standard methods from mulch and were added with water. The entire experiment, which included 5 growth cycles, was 3000 days long; plants were not grown on the substrate for 98 days. Samples of substrate and plant roots were taken for microbial analysis after each growth cycle and also after the intervals between growth cycles. Koch's method was used to determine the total number of microorganisms. Meat peptone agar was used as a nutritive substrate for heterotrophic bacteria. Actinomycetes were grown on starch ammonia agar; fungi on a Czapek medium; and oligonitrophils on nonconcentrated Ashby medium. The method of limiting dilutions was used to perform group analysis of the following functional groups of microorganisms: ammonifying, denitrifying, cellulose-decomposing, and nitrifying. Quantitative analysis of the first three groups was conducted 5-7 days after inoculation, while the nitrogen-fixing group was studied 3 weeks after inoculation. Identification of pure cultures of microorganisms considered morphological and physiological/biochemical features. Data were processed statistically.

It was found that neither light periods not size of balkaniya substrate granules affected concentrations of heterotrophic bacteria, which fluctuated from 1.6 to 6.5 million per gram of substrate. However, increasing granule size affected root microflora, increasing bacteria from 9 to 38 million with a 12-hour period of light and from 6.7 to 154 million on 1 g root with a 16-hour light period. Size of granule and light period did not affect quantity of fungi, either in the substrate or on the roots. Quantity of fungi did not exceed 71,100 per gram substrate or 4800 per gram root. Microflora belonged to the *Aspergillus, Penicillum, Fusarium*, and yeasts. Actinomycetes developed especially rapidly with a 12-hour light period, regardless of granule size of the substrate. Decrease in light period increased nitrogen fixation from 2500 per 1 g root with a 16-hour photoperiod to 6 million per 1 g root with a 12-hour period.

Use of the substrate decreased the bactericidal effects of the preserved water. When the substrate was used for a sustained period, the total number of microorganisms as well as of the bacterial heterotrophs decreased, with the exception of the condition where silver ions had been removed from preserved water. In all cases, predominant bacteria after the fifth growth cycle was *Streptomyces,* while earlier the major rhizospheric microflora had been gram-negative bacteria. This suggests "depletion" of the substrate, probably due to accumulation of antibiotic substance from the streptomyces and mold fungi. Adding humate to the substrate increased the variety of microbes in the rhizosphere. Ammonifying bacteria, which participate in transformation of nitrogen-containing substance, were the most numerous. They decreased with continued use of the same substrate, especially where humate was used. Ammonifying bacteria increased in the interval between growth cycles. Denitrification was particularly pronounced when humate and preserved water were used, but the number of denitrifying bacteria decreased sharply after the fifth growth cycle on humate. In all conditions number of oligotrophilic bacteria decreased after the third growth cycle and subsequently increased. Level of fungi was independent of use of humate or preserved water. Some differences in species were identified in the different conditions. The authors conclude that the use of humates and preserved water facilitates maintenance of microbial activity in the rhizospheres of plants cultivated on balkaniya substrate.

Table 1: Substrate microflora during long-term cultivation of lettuce

Table 2: Species composition of substrate bacteriocenoses as a function of cultivation conditions

Table 3: Physiological groups of microorganisms in the substrate during long-term cultivation of lettuce

PAPERS:

P1065(23/89)*Pospisilova I, Pospisil M (Czechoslovakia), Serova LV.
Collagen metabolism in the skin and bone tissue of rats after a 7-day space flight.
Kosmich eskaya Biologiya i Aviakosmicheskaya Meditsina.
23(2): 44-48; 1989.
[28 references; 15 in English]

Musculoskeletal System, Metabolism, Collagen, Bones, Skin
Rats
Space Flight, Cosmos-1667

Abstract: This study looked at effects of a 7-day space flight on COSMOS-1667 on collagen metabolism in skin and bone tissue. Subjects were a group of 7 3-month-old male Wistar rats maintained in a common cage during flight. A synchronous and two vivarium control groups were also examined. The synchronous control condition and its comparable vivarium group were run 1 month after the flight group. On the day of reentry, flight animals were decapitated, skin (without hair) was taken from the animals' backs, and femur bones were cleaned of bone marrow. Tissue samples were frozen in liquid nitrogen, mechanically homogenized, and infused with pepsin to produce pepsin-soluble and insoluble fractions of collagen, which were separated centrifugally. The insoluble fraction was lyophilized and hydroxyproline, the specific amino acid of collagen, was measured in some samples. The majority of samples were processed with cyanogen bromide, which decomposes collagen into type I and type III peptides, which were measured chromatographically. The pepsin soluble collagen fraction was neutralized and salted to a concentration of 20% NaCl. The sediment was dissolved in an elution buffer solution (50 mM tris-HCL pH 7.5). In a portion of the samples, hydroxyproline was measured to establish the amount of pepsin-soluble collagen. The majority of samples were subjected to zonal precipitative chromatography for separation of collagen I and III and noncollagen proteins (glycoproteins) The amount of collagen was estimated by finding the concentration of hydroxyproline, and in the amount of glycoproteins by determining the concentration of protein.

Flight rats displayed a reliable decrease in concentration of collagen in bone compared to all control groups. In this group, the concentration of pepsin-insoluble collagen decreased, while pepsin-soluble collagen increased. The quantity of glycoproteins per 100 μg hydroxyproline in the soluble fraction was the same in the experimental and synchronous control groups. In the two vivarium control groups, most of both fractions of collagen belonged to type I, while type III was absent in the pepsin-insoluble fraction and virtually absent in the soluble fraction. In the bone tissue of flight animals, type II collagen made up 11% of the soluble fraction and 30% of the insoluble one. Differences with the control group were significant.

There was no difference in the total amount of hydroxyproline in the skin of control and flight animals. However, in the flight group the amount of pepsin-soluble collagen was depressed, while pepsin insoluble collagen was elevated. These results were opposite to those obtained for bone. The amount of glycoproteins per 100 μg hydroxyproline was significantly higher in flight animals. The amount of type II collagen in the pepsin soluble fraction of skin collagen was 0.5% in vivarium controls, 1.5% in synchronous controls, and over 4% in flight animals. In the pepsin insoluble fraction, percent of collagen did not exceed 5% for the control groups, but was over 37% in the flight group.

The authors conclude that the results show that short-term space flight can have significant effects on collagen metabolism in the skin and bones of rodents. Elevated amounts of type III collagen are considered particularly important, since they are systemic, i.e. occurred in both skin and bone. Type II collagen is characteristic of embryonal tissue and certain bone diseases. No explanation is offered for the particular effects observed.

Table 1: Concentration of hydroxyproline in bone tissue and skin of animals

Group	N	Hydroxyproline, µg per 100 mg moist weight pepsin-soluble	pepsin-insoluble	total
		Bone tissue		
Flight	6	146±19	915±45	1061±58
	p_V=0.05	p_V<0.01	$p_{V,S}$<0.05	
		p_S<0.02		
Sync.	5	111±17	1427±109	1538±125
Vivarium	10	90±13	1555±182	1645±185
		Skin		
Flight	7	799±88	1528±194	2327±258
		p_V<0.02	p_V<0.01	
		p_S<0.05		
Sync.	7	1487±309	1184±213	2671±384
			p_V<0.05	
Vivarium	12	1242±155	695±71	1937±203

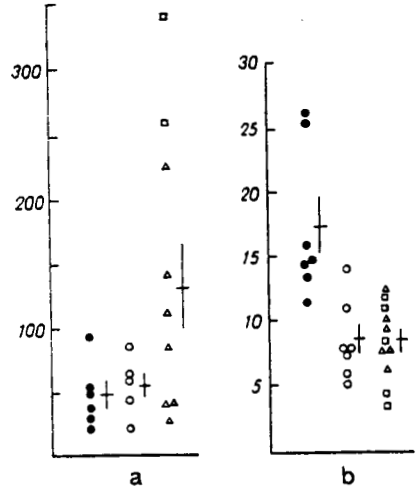
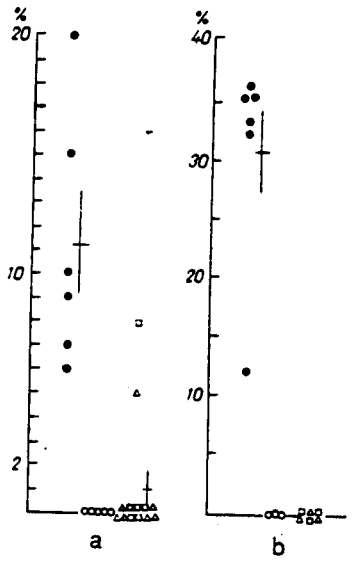


Figure 1: Concentration of glycoproteins in µg per 100 µg pepsin-soluble hydroxyproline in femur bone (a) and skin (b) of rats of the flight and control groups

Here and in figures 2 and 3: filled circles - flight group, empty circles - synchronous control; triangles and squares - vivarium control group.



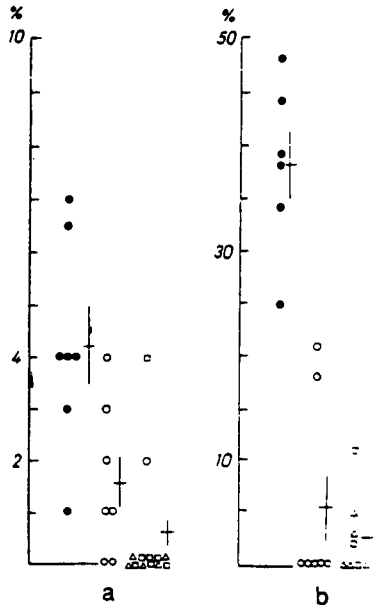


Figure 2: Type III collagen (in %) in pepsin-soluble (a) and pepsin-insoluble (b) fractions of bone tissue of rats in the flight and control groups

Figure 3: Type III collagen (in %) in pepsin-soluble (a) and pepsin-insoluble (b) fractions of the skin of rats in flight and control groups

P1067(23/89)* Burkovskaya TYe Vorozhtsova SV, Gundroina SF, Nazarov VM, Frontas'yeva MV.
The composition of bone tissue in mice in the norm and during hypokinesia.
Kosmich eskaya Biologiya i Aviakosmicheskaya Meditsina.
23(2): 51-55; 1989.
[29 references; 2 in English]

Musculoskeletal System, Bone Tissue, Composition, Femur, Parietal Bone, Ectopic Bone, Demineralization, Mineral Metabolism
Mice
Hypokinesia

Abstract: In this experiment, a sample of bone marrow from the femur of a normal donor was implanted under the kidney capsule of anesthetized male mice. A mean of $1.3 \cdot 10^7$ cells was introduced in this way. Starting on on days 5-6 after implantation, 37 mice underwent a 3-week period of hypokinesia in individual immobilization cages. An additional 120 mice were maintained under ordinary laboratory conditions after implantation. After 1 month the animals were sacrificed and their parietal and femur bones isolated and cleaned of marrow. Ectopic bone developing at the implantation site was also removed. In addition, material was taken from mice not undergoing the implantation operation but submitted to 3 or 7 days of hypokinesia. Concentrations of calcium, phosphorus, sodium, magnesium, iron, rubidium, ruthenium, zinc, cobalt, chromium, strontium, bromine, and antimony were measured by neutron activation analysis.

When the distribution of the 13 elements was analyzed in the parietal, femur, and ectopic bones of normally treated mice, little difference was found among the three types of bone in the macroelements Ca and P. However, interbone differences did exist in the remaining trace elements. In particular, bones having an antigravity function (femur) contained 6 times more Sr, 4 times more Fe, and 1.5 times as much Br, Zn, and Cr as bones not serving this function (parietal) Ectopic bone did not differ significantly from skeletal bone in its composition. However, there was a tendency for it to contain more trace elements (Fe, Ru, Zn, Sb) that act as activators of the enzymatic systems and catalysts of physical and chemical bone-formation reactions. Animals submitted to hypokinesia formed only half as much ectopic bone by weight as animals permitted to move freely. Differences in element distribution were noted both in skeletal and ectopic bones, but were more pronounced in the former. With regard to changes over the hypokinesia period the following types of dynamics could be distinguished: 1) progressive loss of the element from bone (Ca, P, Mg, Fe); 2) progressive inclusion of the element in bone tissue (Sr); 3) temporary loss of the element from bone followed by its restoration (Zn, Cr, Ru, Rb, Na, Sb); 4) changes in different directions in the parietal and skeletal bones (Br, Co). The elements lost during hypokinesia were those that normally predominate in bone tissue. This demineralization was accompanied by very substantial increase in Sr, an element close to Ca in physical and chemical properties and which competes with it in the crystal matrix of hydroxyapatite. This element increased by a factor of 2 in parietal and ectopic bone and by a factor of 6 in the femur. It is suggested that this change is facilitated by increased activation of the pituitary-adrenal system in the first phase of adaptation. Changes in other trace elements are attributed to activation of various hormonal and enzymatic systems during the initial phase of the adaptation syndrome. The authors conclude that due to their rapid metabolic rate, mice are suitable subjects for the study of mineral metabolism in bone.

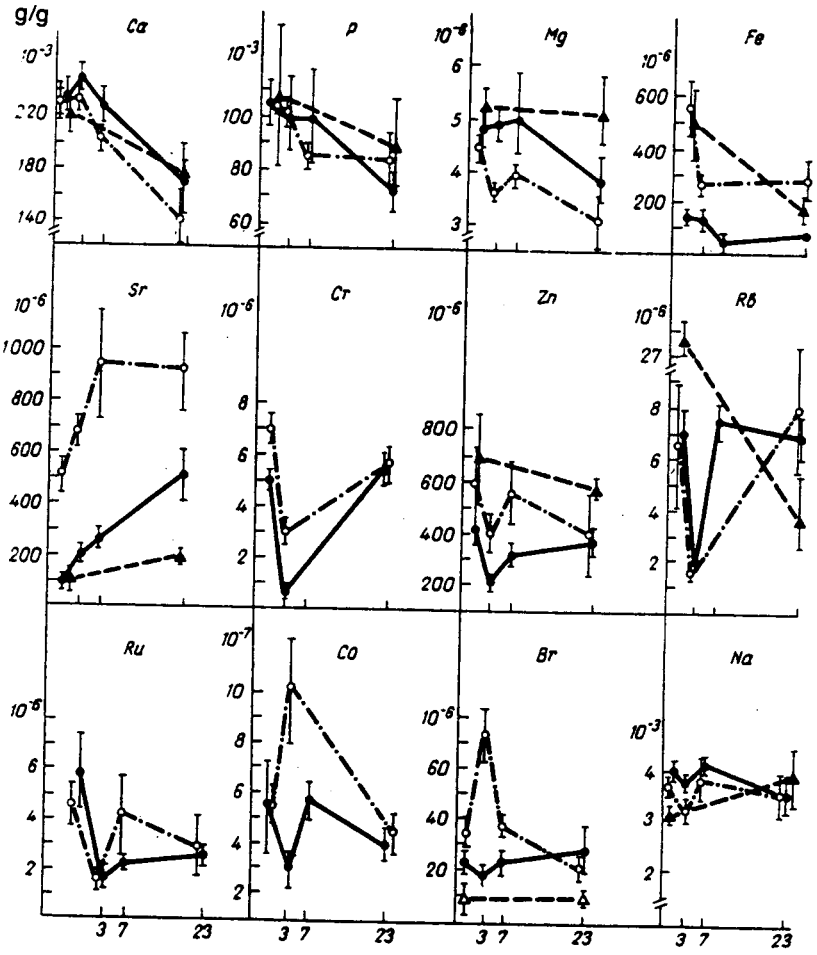


Figure 1: Changes in concentrations of elements in bone tissue of mice undergoing hypokinesia

Abscissa: days; ordinate: g/g; empty circles - femur bones; filled circles -- parietal bones; filled triangles · ectopic bones. Points at the beginning correspond to concentration of each element in the bones of control mice

Figure 2: Effects of hypokinesia on the size of ectopic bone and the site of ectopic hemopoiesis

NEUROPHYSIOLOGY

PAPERS:

P1077(23/89)* Drozd YuV, Puko VM, Ryumin Yul.
Permeability of the blood-brain barrier in simulated motion sickness.
Kosmicheskaya Biologiya i Aviaskosmicheskaya Meditsina.
23(2): 88; 1989.
[5 references; 2 in English]

Neurophysiology, Blood-Brain Barrier, Permeability
Mice, Male; Cats
Motion Sickness, Simulated; Alpha-Tocopherol

Abstract: The permeability of the blood-brain barrier was assessed in 100 mature male F_1 mice. Acid fuchsin solution was injected intraperitoneally in 25 control and 25 experimental mice. Passage of this substance through the blood-brain barrier results in generalized convulsion, followed shortly by death. Immediately after injection the experimental animals were submitted to a motion-sickness-inducing procedure. The time before convulsions and survival time were recorded for both groups. Mean time to convulsion in experimental and control animals was 67±5 and 64±2 minutes, respectively; mean survival time was 98±19 and 88±15 minutes, respectively.

An additional experiment replicated the first, but animals were first injected subdurally with 1 mg of an oil solution of alpha-tocopherol. Time before convulsion was 81±20 and 77±15 minutes for the experimental (motion sickness) and control groups, respectively. Survival time increased to 134.6±31.1 and 109±28.2 minutes, respectively. The authors conclude (with unclear justification) that alpha-tocopherol can to some extent prevent the disruption of blood-brain barrier permeability associated with motion sickness.

To confirm this, motion sickness symptoms were studied in 6 cats after administration of alpha-tocopherol. Rated symptoms decreased from 13.6 in the baseline condition to 4.0 after vitamins. The authors conclude that the vestibulo-protective effect of alpha-tocopherol is associated with stabilization of blood-brain barrier permeability.

P1087(23/89) Zhuravleva NG.
Restructuring of bioelectric activity of the brain during adaptation to long-term hypokinesia.
Gigiyena i Sanitariya.
1989(2): 32-35.
[17 references; 2 in English]

Neurophysiology, Bioelectric Activity, Brain
Rats, Males
Adaptation, Hypokinesia, Long-Term

Abstract: This work studied changes in total bioelectric activity of the brain in 41 male rats confined in immobilization cages for 23 hours per day, 5 times a week for 7-8 months. Amplitude frequency curves were obtained for the averaged visual evoked potential to an indifferent stimulus. Total background activity was also recorded, as was the EEG component of the orienting reflex to a series of tones of 500 Hz, and response to rhythmic photostimulation at a frequency of 1-25 Gz. Electrodes were implanted in the cortex and limbic-reticular complex. EEG and the visual evoked potentials were measured on various days beginning approximately 10 minutes after injection with d-tubocurarine (1.2 mg/kg), with the animals put on a respirator and dark adapted.

The major results attributable to hypokinesia were decrease in the overall level of bioelectric brain activity and compensatory increase in reactivity to exogenous signals. The author claims that decreased general activity is mainly due to increases in generalized backward inhibition of neural activity, while the increased reactivity is attributed to enhanced brain synapse function. Changes are concluded to be organic, rather than functional, in nature since they cannot be diminished by procedures increasing brain tonus [preliminary electrical stimulation of the reticular formation]. Negative effects of these processes are predicted to involve decreases in the functional capacity of the brain and increase in the physiological response to stimuli, which, in combination, could lead to asthenization in a high pressure situation.

Figure 1: Baseline differences in EEG in control rats and rats undergoing long-term hypokinesia

Figure 2: Visual evoked potentials in control rats and rats undergoing long-term hypokinesia, and changes in them after preliminary electrical stimulation of the reticular formation

Figure 3: Differences in changes in EEG rhythms in control rats and those undergoing long-term hypokinesia

Figure 4: Changes in extinction curves for the EEG component of the orienting reflex in control rats and those undergoing long-term hypokinesia

P1090(23/89)Devyatkina TA, Tarasenko LM.
Dependence of lipid peroxidation on nervous system type and endurance of physical exercise.
Fiziologicheskiy Zhurnal.
35(2): 55-59; 1989.
[15 references; none in English]
Authors' Affiliation: Poltava Medical Stomatological Institute, Ukrainian Ministry of Health

Metabolism, Lipid Peroxidation; Endocrinology, Adrenal Gland, Hypothalamus; Brain
Rats, Males
Neurophysiology, Nervous System Type; Exercise Endurance

Abstract: This research was performed on 49 male Wistar rats which had been divided into three groups on the basis of nervous system type (excitation-dominant, inhibition-dominant, stable). Group assignment was based on animals' behavior in an "open field" test. All animals were subjected to graded physical exercise involving running on a treadmill at 18-20 m/min daily for 30 days. Animals matched for nervous system type served as controls. Lipid peroxidation in tissues was assessed on the basis of accumulation of malonic dialdehyde (MDA) and activity of superoxide dismustase (SOD). Condition of periodontal bone tissue was assessed on the basis of concentration of calcium and amount of baring of molar roots, and index of resorption of the alveolar process. Endurance of physical exercise was estimated on the basis of frequency, severity, and number of stomach ulcers, ratio of adrenal gland weight to that of the kidneys, and also extent of resorption of periodontal bone.

Exercise affected lipid peroxidation differently in different tissues. Greatest decreases in SOD activity were observed in the hypothalamus and adrenal glands of excitation-dominant rats. Stable animals showed decreased activity of this enzyme in the hypothalamus, but no changes in the adrenal gland. Inhibition-dominant animals did not display changes in these parameters. In excitation-dominant animals, lipid peroxidation increased significantly in the brain in response to exercise, as revealed by significant accumulation of MDA. This parameter did not change as much in the other two types, suggesting stronger antioxidant protection, preventing activation of lipid peroxidation in the brain. Animals of the excitation-dominant and stable types showed similar patterns of stomach ulceration, while ulceration was minimal in the inhibition-dominant type. Excitation-dominant animals showed a tendency for calcium to decrease in periodontal bone and a decrease in relative weight of the adrenal gland. Other groups did not display these changes.

The authors conclude that endurance of physical exertion is determined by lipid peroxidation, which depends on typological characteristics of the nervous system. The results obtained attest to the need to select exercise schedule or prescribe antioxidants for an individual on the basis of reactivity type of the individual nervous system.

Table 1: Effects of physical exercise on activity of SDO in rat tissues

Table 2: Effects of physical exercise on concentration of MDAin the brain of rats

Table 3: Parameters of endurance of physical exercise in rats with different types of nervous systems

NUTRITION

PAPERS:

P1068(23/89)*Sivuk Akin Abakumova IA, Gur'yeva TS, Gryaznova VN, Korshunova VA, Mosyakina LI, Tret'yakova VA, Tresvyatskaya NA, Khokhlova OS.
The effects of vegetable food products (carrot and radish tops) on certain metabolic parameters in humans.
Kosmich eskaya Biologiya i Aviakosmicheskaya Meditsina.
23(2): 56-59; 1989.
[29 references; 2 in English]

Metabolism
Humans, Males
Nutrition, Vegetable, Carrots and Vegetable Tops

Abstract: Nine male volunteers took part in this experiment, which lasted 28 days. During that time group 3 ate a standard diet, group 1 ate the same diet with the addition of 75 g of radish tops per day, while group 3 ate a like amount of carrot tops. The greens were chopped and served with salt and vegetable oil. Metabolism was assessed by measuring the concentrations of total and aminized nitrogen, urea, creatinine, and uric acid in daily urine every 3 days. Venous blood was taken on days 15 and 20 and concentrations of total protein, total lipids, cholesterol and blood sugar were measured. Composition of peripheral blood was also determined.

All subjects reacted positively to the taste of the greens. Subjects tended to lose weight on the diet with or without greens. No significant differences were noted in biochemical parameters of blood. There was a tendency in all three groups for total protein in blood serum to decrease, although remaining within normal limits. In group 1 (note: the pairing of vegetable and group number is different in the "procedure" and "results" sections; apparently lipids increased in the carrot top group) there was a tendency for total lipids to increase in blood, while this parameter remained the same. Subjects given the supplemental greens displayed a significant increase in the number of monocytes, a reaction to accumulation of nonmetabolized products. Total leukocytes decreased significantly, as did hemoglobin, possibly signalling an inadequate supply of amino acids. Subjects receiving additional nutrients displayed increased excretion of total nitrogen and nitric amines. The ratio of nitric urea to total nitrogen in urine is an indirect criterion of the biological value of protein ingested, reflecting the rate of peraminization of amino acids ingested. This ratio did not differ significantly for the three groups. The authors conclude that the use of radish and carrot tops in the human diet, in an amount of 75 g per day, does not induce any adverse changes in the metabolic parameters investigated, suggesting the suitability of these products as components of cosmonauts' diets.

Table 1: Concentration of major nutrients in 100 g of greens

Table 2: Morphological composition of the blood of subjects eating the plant biomass

Table 3: Renal excretion of end-products of nitrogen metabolism in subjects consuming plant biomass

PAPERS:

P1082(23/89) Cherkasov GV, Yurova KS.
Acid-base balance of the blood of rats exposed to a constant magnetic field.
Kosmicheskaya Biologiya i Aviaskosmicheskaya Meditsina.
23(2): 95; 1989.
[11 references]
Translation of abstract on file with the All-Union Institute of Scientific and Technical Information and the All-Union Scientific and Research Institute of Medical Information

Hematology, Acid-Base Balance, Blood Gases
Rats
Radiobiology, Magnetic Field, Constant

The goal of this work was to evaluate a number of parameters of acid-base balance and the gas composition of arterial and venous blood under conditions of exposure to a constant magnetic field. The research was conducted with 28 outbred male rats weighing 260-300 g. The magnetic field was created using an SP-15A magnet. Immediately after a 3-hour exposure session to a constant magnetic field of 0.4 Tl, acid- base balance and gaseous composition of the blood were measured. The micro-Astrup method was used, with the "ABL 2 Acid-Base Laboratory" manufactured by the Danish firm "Radiometer." Under urethane anesthesia arterial blood was removed from the abdominal section of the aorta and venous blood from the dorsal vena cava. The arterial blood parameters did not undergo changes under exposure to the magnetic field and did not differ from data in the literature. While acid-base balance was not affected in venous blood, there was a small but significant (91.2% of control, $p<0.02$) decrease in pO_2. The percent of oxygen saturation in venous blood correspondingly decreased from 84.9±1.0% in the control to 81·±1.4% ($p<0.05$). The increase in the arterial-venous difference in oxygen suggests that exposure to a constant magnetic filed affects oxygen homeostasis. Decreased pO_2 in venous blood accompanying unaltered amounts in arterial blood should be considered a result of increased utilization of oxygen by the tissues. In response to exposure to the constant magnetic field, changes occur in tissue metabolism that are evidently indicative of increased oxygen requirements.

P1085(23/89)Fedorenko BS, Parfenov YuD, Batkay L.
Relative biological effectiveness of accelerated particles based on death rate of animals
Kosmicheskaya Biologiya i Aviaskosmicheskaya Meditsina.
23(2): 96 ; 1989.
[18 references]

Radiobiology, Relative Biological Effectiveness, Death Rate
Rats, Mice
Accelerated Ions, γ-Radiation

Translation of abstract of paper on file with the All-Union Institute of Scientific and Technical Information and the All-Union Scientific and Research Institute of Medical Information

An analysis of the relative biological effectiveness of accelerated helium ions with energy of 5 HeV/nuclon and protons of ^{9}HeV compared to ^{60}Co γ-irradiation, was effected by studying death rates of small laboratory animals. The animals were irradiated at doses of 3.0 to 10.0 Gy and death rate was computed for the 30 days subsequent to exposure to radiation. Relative biological effectiveness of helium ions on the basis of a $LD_{50/30}$ criterion was 1.23 for mice, while for protons in an experiment on rats this value was 1.27. This increase in the effectiveness of accelerated particles is not statistically significant. However, if one considers the parameter b of the linear equation determining the slope of the straight line as the death rate for a unit dose (in log transform), one sees that the higher the value of b, the higher the effectiveness of the given radiation based on the frequency of death after a unit dose. Relative biological effectiveness may thus be expressed as the ratio $b(\alpha)/b(\gamma)$. For helium ions this ratio is equal to 1.25 and for protons to 1.91. This attests to a higher biological effectiveness for charged particles compared to γ–radiation based on the short-term death rate of animals .

P1070(23/89)*Antipov VV, Vasin MV, Gaydamakin AN.
Species-specific responses of lymphocyte succinate dehydrogenases to acute hypoxic hypoxia in animals and their association with radiation tolerance.
Kosmicheskaya Biologiya i Aviaskosmicheskaya Meditsina.
23(2): 63-66; 1989.
[8 references; none in English]

Hematology, Lymphocyte Succinate Dehydrogenase; Metabolism, Rate
Mice, Rats, Dogs, Species Specificity
Radiobiology, Radiation Tolerance, Hypoxia

Abstract: This study involved a comparative analysis of changes in radiation tolerance induced by acute hypoxic hypoxia as a function of hypoxia severity in animals differing in basal metabolic rate. Activity of succinate dehydrogenase (SDH) in lymphocytes was used as an indicator of severity of hypoxia. Subjects were 685 white outbred female mice, 465 white outbred female rats, and 12 dogs of both sexes. The rodents were irradiated with γ-quanta of ^{60}Co in doses of 7.0-15.0 Gy at a dose rate of 2.77-2.99 Gy/min. They were placed in an acrylic chamber into which was pumped air or a hypoxic gas mixture (N_2+O_2) with oxygen concentration of 5, 7, 8, 10 12, or 15% oxygen. The dogs were irradiated with ^{60}Co at a dose of 4 Gy with a dose rate of 0.14-0.16 Gy(per min?). These animals were restrained in a wooden box and air of a hypoxic mixture (5.8 or 10% O_2) was inhaled through a device fitted to the animals muzzle. Changes in radiation tolerance were assessed on the basis of animals survival rate over a 30-(rodents) or 60-day period (dogs) after irradiation and the mean survival time of the animals that died. Activity of succinate dehydrogenase (SDH) in lymphocytes of peripheral blood was determined cytochemically (number of granules of formazan per lymphocyte) before and 1, 2, 3, 4, 6, 8, 10, 12, and 15 minutes after exposure to the hypoxic mixture Rate of increase in SDH activity in lymphocytes (V SDH) was established by dividing the greatest increase in SDH activity in percentage of baseline (ΔA%) by the time to attain that peak activity: ΔA %/t. $LD_{50/30}$ of γ -quanta of ^{60}Co and the dose reduction factor (DRF) were computed. Regression analysis was used to develop an equation relating the parameters.

In rats and dogs, exposure to certain hypoxic mixtures gave rise to periodic twofold increases in activity of SDH in lymphocytes. At lower levels of hypoxia, V SDH was lower and the oscillation period of enzyme activity was greater. When breathing the same hypoxic mixture, rats manifested a stronger, quicker SDH reaction than dogs. The difference is related by the authors to the lower oxygen need in larger animals. The authors further believe that tolerance of acute hypoxia is closely related to radiation tolerance of the animal in a hypoxic state. Animals with higher levels of oxygen consumption, and therefore, poor hypoxia tolerance, showed greater increases in endurance of ionizing radiation in a hypoxic state. Hypoxic mixture had a 1.5-2 fold greater antiradiation effect in mice than in rats, and the oxygen consumption of the two species differed in approximately the same ratio. A regression equation was derived relating the dose reduction factor of a hypoxic medium to its concentration of oxygen. Another equation can be derived relating the rate of increase in SDH activity to the oxygen content of the mixture for a given species. For each species, then, a relationship between the dose reduction effect of a mixture and the rate of increase of SDH activity in blood can also be found. This relationship reflects the intensity of the cellular reaction to acute hypoxia as manifested in the development of the earliest and most sensitive adaptive mechanism of response to oxygen insufficiency, related to inclusion of the SDH system. This formula is: DRF of hypoxic mixture = 0.97+0.215 (V SDH). When V SDH data for dogs were plugged into this formula, predicted increase in radiation tolerance due to a given hypoxic mixture accorded well with empirical results.

Table: Effect of breathing a hypoxic mixture on SDH activity in blood lymphocytes in rats and dogs

Figure 1: Change in SDH activity in blood lymphocytes in rats and dogs after breathing a hypoxic mixture with varying percentages of oxygen

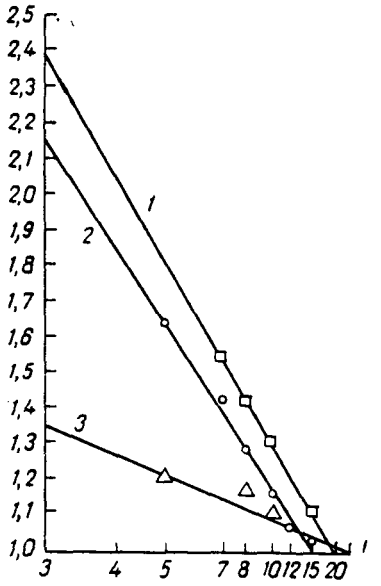


Figure 2: Antiradiation effect of a hypoxic mixture as a function of its concentration of oxygen

Abscissa: oxygen concentration in the hypoxic mixture; Ordinate: dose reduction factor of mixture. 1 - mice, 2 - rats, 3 - dogs

Figure 3: Antiradiation effect of a hypoxic mixture as a function of the level of oxygen consumption of the organism

P1079(23/89)* Vorozhtsova SV, Savinskiy AK,
RBE of fission neutrons at low doses as reflected in cytogenetic changes in the cells of the corneal epithelium in mice.
Kosmicheskaya Biologiya i Aviaskosmicheskaya Meditsina.
23(2): 91-93; 1989.
[2 references; none in English]

Cytology, Cytogenetic Changes, Cornea
Mice
Radiobiology, Relative Biological Effectiveness, Fission Neutrons, Low Doses

Abstract: Because of the potential use of nuclear reactors as energy sources on spacecraft, it is important to understand the biological effects of fast neutrons. The present experiment exposed male mice to whole body irradiation with fast neutrons.at doses ranging from 0.125 to 2 Gy. Neutrons were generated by a pulse reactor working in the booster mode. Dose rate was 0.02 Gy/min. Contribution of γ irradiation did not exceed 10% . Neutron spectra were measured by a scintillation spectrometer. For the spectrum used, mean linear energy transfer in soft tissue was 37.8 keV/μm. Fast neutron irradiation was compared to γ-irradiation from ^{60}Co with dose rate of 0.06 1 Gy/sec. Aside from one-time doses of radiation, subjects underwent fractional irradiation with a 24-hour interval between fractions. At periods of 24, 72, and 120 hours and 1 and 3 months after exposure to radiation, animals were decapitated. The whole cornea was prepared and stained with hematoxylin. Radiation damage to cells of the corneal epithelium was assessed on the basis of disruption of the proliferative activity of the process of cell divisions. The criterion used was the induction of aberrant mitoses in the form of bridges, bridge fragments, and both together at the stage of the late anaphase and early telophase. A total of 800 mice were used.

Neutrons and γ-irradiation induced the same kinds of changes in the chromosome apparatus of epithelial cells. However, fast neutron irradiation led to a greater number of aberrant mitoses than did γ-irradiation. Their induction depended on dosage and elapsed time since irradiation. At doses up to 0.5 Gy the curve was close to linear, but at doses of 1-2 Gy the curve lost its linearity. There were no significant differences in the changes caused by neutrons and γ-irradiation. Fractionated γ irradiation, however, was associated with fewer damaged cells than single-dose irradiation, although these differences were not significant. Two models were used to approximate the experimental data:

$$\text{Model A: } E(D,t)=1-\exp(-\alpha D);.$$
$$\text{and Model B: } E(D,t)=\beta D \exp(-\gamma D),$$

where E(D,t) is the induction of aberrant mitoses in cells of the corneal epithelium of mice at dose D at time t after irradiation; α, β and γ are free parameters. The values of RBE for low doses of neutron based on the criterion of induction of aberrant mitoses in cells of the corneal epithelium of mice are virtually independent of elapsed time after treatment and fractionation of dose and are only weakly dependent on the model used, equalling on the order of 7.0±1.5.

Figure 1: Induction of aberrant mitoses in cells of the corneal epithelium of mice as a function of dose at various times after single irradiation with neutrons and γ-irradiation

Figure 2: Induction of aberrant mitoses in cells of the corneal epithelium of mice as a function of dosage 24 hours after a single or fractionated dose of neutrons and γ-irradiation

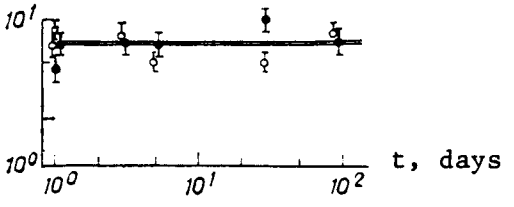


Figure 3: Value of the RBE for neutrons of the fission spectrum at low doses (<0.01 Gy) as a function of time after irradiation

Empty and filled circles are single dose irradiation for models A and B, respectively; empty and filled squares are fractionated irradiation for models A and B, respectively

BOOK REVIEW:

BR16(23/89)* Ryshov AI, Logvinov SV.
Review of : Davydov BI, Ushakov IB.
Ионизирующие Излучения и Мозг: Поведенские и Структурно-Функциональные Паттерны
Ioniziruyushchiye Izlucheniya i Mozg: Povedenskiye i Strukturno-Funktsional;nyye Patterny
[Ionizing Radiation and the Brain: Behavioral and Structural/Functional Patterns;]
Moscow: Radiatsionnaya Biologiya, vol 8, 1987, 336 pages.
Kosmicheskaya Biologiya i Aviaskosmicheskaya Meditsina.
23(2): 93-94; 1989.

KEY WORDS: Radiobiology, Ionizing Radiation, Neurophysiology, Brain, Psychology, Behavior, Human Performance, Work Capacity, Humans, Animals

Review: The psychophysiological effects of ionizing radiation on the central nervous system are directly related to predicting human work capacity in jobs with significant radiation risk, especially under conditions of space and aircraft flight. The brain is the most resistant organ to the effects of radiation, and yet, at the same time, is a highly reactive physiological system with which radiobiology has been concerned for many decades, and which remains at the present time a radiobiological mystery. The dispute concerning the meanings of the concepts of "structure" and "function," continuing in neuroradiobiology and neuropathology in general until the recent past and the, sometimes unfounded, interpretation of changes in the functioning of the brain as "purely functional," devoid of any structural basis, have not been conducive to rapid development of an understanding of the subtle mechanisms underlying radiation effects on the central nervous system. For this reason, the book being reviewed here is one of the first major works to summarize and analyze the set of behavioral, neurological, morphological, and biochemical aspects of the problem of the effects of ionizing radiation on the brain.

The use of the term "pattern" in the title suggests a phenomenological presentation of observed radiocerebral effects. At the same time, by the organization of the chapters of the monograph, and the order in which the material is presented -- beginning with psychophysiological behavioral investigations and ending with subtle ultrastructural and neurochemical reactions of nerve tissue -- the authors invite the reader to analyze the deep mechanisms of the postradiation process in the CNS.

The first two chapters of the book are devoted to the behavioral physiology of the irradiated individual. Psychophysiological investigations of people exposed to ionizing radiation are relatively rare, but at the same time very valuable. Behaviorally significant symptoms of irradiated individuals in emergency situations are considered from the point of view of predicting psychological and physical human work capacity, which is important for simulating certain aspects of space and aircraft flight.

Behavioral reactions in animals are considered for a broad range of radiation doses, which compensates to some degree for the relative deficit of studies on irradiated humans. Considering the limits of extrapolation of experimental animal data to humans, the authors focus on the radiation psychophysiology of primates, and consider the mechanisms underlying learning and memory, the effects of decreasing attention span, and elements of operator performance in irradiated monkeys. In addition, they present a detailed analysis of interspecies differences in experiments on dwarf pigs, dogs, cats, and rodents; and a picture of early transient "incompetence," which has a number of properties. The authors conclude that the "nucleus" of the whole spectrum of postradiation behavioral changes is

biological motivation. Ionizing radiation alters both the motivations themselves, and the interactions among them. At the same time, the neurological and behavioral patterns described once again convince the reader of the great compensatory capacities of the brain.

Changes in cerebral hemodynamics, considered in Chapter 3 , play an important role in the genesis of neurological effects of radiation. The authors analyze overall hemodynamics and cerebral blood flow, drawing temporal and dose-associated parallels with manifestations of transient "incompetence" and other behavioral reactions, and raise the issue of the neurochemical mechanisms of hemodynamic disruptions. In this same chapter they cite data from recent *in vivo* and *in vitro* electrophysiological studies. The authors consider the bioelectrical reactions not only of the brain, but also those in the peripheral components of the visual and auditory system, where radiation effects effects could have significantly disrupt operator performance.

Chapter 4 considers the structural bases of early disruptions of the permeability of the brain-blood barrier and their role in postradiation reactions of nerve tissue. The authors analyze the structural changes in the major components of the brain-blood barrier the endothelium, perivascular astrocyte, and consider changes in others, such as the basal membrane, in less detail. The authors touch on the role of tissue basophils in these processes, a question which has only been raised relatively recently and is still open to debate, as is the very presence of tissue basophils in brain tissue. For this reason, appropriate illustrations would have allowed a deeper treatment of this issue.

The merits of this book include the logical sequence in which the material is presented and the parallel analysis of structural and functional parameters, providing an overall picture of the postradiation process in the CNS. In Chapter 5, after a description of the brain-blood barrier, the authors logically consider the fluid-electrolyte profile of the brain after irradiation and the morphological manifestations of the electrolyte imbalance that occurs. The material from studies of the synaptic system, one of the most affected components of the nervous system, is very valuable. However, the data from neurochemical investigations are currently insufficient to support unambiguous conclusions on the destruction of any neuromediating synaptic system, but attest to the early polymediator effects of ionizing radiation.

In Chapter 6, the authors discuss a wide range of neurochemical changes in the brain after irradiation. In particular, they focus on the parameters of biochemical metabolism of nucleic acids and nucleotides, and also polyneuromediators, including cholinergic effects, noradrenergic, dopaminergic, and serotinergic systems.

Ionizing radiation rarely acts as an isolated factor, but affects the organism in combination with other external agents. Chapter 7 considers the radiomodifying effect of microwave radiation, altered gas media, and various drugs, including radioprotectors. The problem of the combined effects of ionizing radiation and other factors is, without a doubt, still inadequately understood. This makes this chapter of the monograph particularly interesting, since it deals with combined effects on the most radioresistant system -- the brain.

Chapter 8 discusses the status of a very important, but little studied question, having to do with the effect of radiation on a fetus. Neuroembryological investigations have a history of almost 60 years; nonetheless, this problem merits further attention, since the magnitude of radiation risk for a fetus is extremely high. Of special practical value in this section is the material on pharmacological protection of the fetal brain from the harmful effects of various doses of ionizing radiation.

The monograph ends with a short conclusion and a very extensive list of cited references, numbering more than a thousand titles.

On the whole, Davydov and Ushakov's book reflects a comprehensive, multilevel (from behavioral reactions to morphochemical properties) approach to the study of the complex area of CNS radiobiology. Considering the novelty and value of the empirical material and the persuasiveness of the conclusions, one can confidently predict that the book will be of interest to a wide range of neurophysiologists and other specialists working in radiation medicine.

REPRODUCTIVE SYSTEM

PAPERS:

P1058(23/89)* Serova LV.
The effect of weightlessness on the mammalian reproductive system.
Kosmicheskaya Biologiya i Aviaskosmicheskaya Meditsina.
23(2): 11-15 ; 1989.
[40 references; 11 in English]

Reproductive System, Reproductive Function, Impregnation, Abortion, Mating, Estral Cycle, Sperm; Genetics, Mutations; Developmental Biology
Rats, Male, Female
Space Flight, COSMOS-605, -936, -1129, -1514, -1667; Centrifugation; Adaptation

Abstract: It is usually conceded that any new living environment can be considered assimilated by a biological species only if the species retains a normal reproductive function and produces viable offspring. This review article summarizes the admittedly limited data on the effects of space flight on these functions. The first experiment in this area was performed on COSMOS-1129 in 1979. Male and female Wistar line rats were placed in a cage with the sexes separated by a partition that was removed on day 2 of flight. No offspring were attained from this group and events occurring during flight could only be inferred by comparing the weights of the flight females to those of control animals undergoing normal pregnancy and pregnancy with resorption of the fetuses. Such analyses supported a conclusion that during the 18.5-day flight, two of five females were impregnated (compared to 100% in the control group). Spontaneous abortions were thought to occur in response to reentry impact in animals already weakened by exposure to weightlessness. It was hypothesized that the remaining two animals failed to be impregnated because of disruption of the estral cycle, and sexual behavior due to the stress reaction occurring in response to flight conditions. Similar failure of impregnation occurs when animals are exposed to immobilization stress prior to mating.

The next space experiment exposed pregnant female rats to space for 5 days during days 13-18 of pregnancy on COSMOS 1514. In general, results indicated that animals exposed to space for slightly less than 1/4 of their prenatal development period developed posnatally to sexual maturity and produced offspring without any major deviation from the norm. Future experiments will seek to determine the effects of exposure to space during an earlier more sensitive period of prenatal development and then during the entire cycle of pre- and postnatal development, culminating in exposure to space throughout the life cycles of several generations of animals. These experiments will require long-term flights with a trained biologist or physiologist on board.

Studies of the effects of clinostatting during early stages of mammalian development when fetal cells underwent *in vitro* cultivation experiments revealed no differences in course of impregnation or early stages of cleavage. In spite of American plans to use centrifugation to encourage mating, the author believes that mating and impregnation will be possible in weightlessness provided animals undergo preliminary adaptation. A number of Western studies have tried to remove the nonspecific stress component from their experiments on responses to weightlessness using isolated embryos and their organs or, in simulation experiments, preliminary adaptation.

Using hypergravity as a model, the present author, as well as Westerners, have found that if parents undergo preliminary adaptation to weightlessness, their offspring will develop normally. Soviet experiments also suggest that the best time to place males and females

together for the purposes of mating is day 2-3 of exposure to space. The animals will begin to mate only when adaptation is complete. To determine the maximum effects of weightlessness, animals in various stages of the reproductive cycle that have not been preadapted should serve as subjects.

It is also of great interest to investigate the effects of weightlessness on male reproductive function. The first study in this line was published in 1967, when N. L. Fedorova found that two male dogs exposed to space for 22 days had an elevated number of atypical spermatozoa. Histological study of the testes of rats exposed to space for 18-22 days revealed no significant differences from controls (Plakhut-Plakutina). However, rats exposed on COSMOS-936 did show changes in spermatogenesis. In an experiment with male rats flown on COSMOS-605, mated 2.5 months after reentry, offspring of flight animals showed no difference from control. Analogous results were found for rats flown on COSMOS-1129 and mated 2 months after reentry. When mating took place 5 days postflight, no increased pre- or post-implantation deaths took place. However, offspring born in the latter case displayed a number of differences from controls; mainly summarizable as resulting from physiological immaturity.

Reproductive function in male rats exposed to space for 7 days on COSMOS-1667 was studied extensively. No effects were found in testes or their homogenates. No effects on sexual activity were found 2 weeks postflight and females impregnated by flight rats did not differ in the course of pregnancy, litter characteristics, or offspring anomaly or death. No changes were found in the offspring with regard to rate of growth and development, physiological endurance, or behavior. These results differ from those obtained by Americans who found decreased testicular weight and reduced number of spermatogons under similar circumstances.

Lack of changes in cellular elements of spermatogenesis found by Soviets after space flight contrast with changes found in similar preparations of bone marrow. Thus, the cellular elements of spermatogenesis, a system which is very sensitive to various environmental factors, when exposed to weightlessness actually appear more resistant than other continuously renewing cell populations. More research is strongly recommended.

P1042(23/89)Serova LV, Chel'naya, Bryantseva LA.
State of female rats exposed to weightlessness during pregnancy: General state of the animals. Weight of body and organs. Blood Profile.
In: Gazenko OG (editor).
Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages: 38-39.

Developmental Biology, Reproductive System, Hematology; Endocrinology, Adrenals, Thymus, Liver; Kidneys; Myocardium
Rats, Female, Pregnant
Space Flight, Cosmos-1514

Abstract: Pregnant female rats flown on COSMOS-1514 from days 13 to 18 of gestation were studied. Before the flight, the state of the rats was fully satisfactory, their growth was good, and their blood profiles were normal. When the rats were removed from the "BIOS-vivarium" unit on the day of biosatellite reentry, it was noted that their coats and tails were soiled with food. Nevertheless, the state of the animals was satisfactory, they were active and mobile. When some animals were dissected, no pathological changes were noted in the organs of the chest or abdominal cavities, nor were there any instances of damage to the bones of their legs or organs, nor signs of internal bleeding.

During the experiment, between days 13 and 18 of pregnancy, the flight animals gained 5 g in weight, while animals in a synchronous group gained 65 g, as is normal for this period of pregnancy. Consumption of food by animals in the flight and synchronous groups during the flight period was virtually identical, averaging 54 and 57 g per rat per day.

Concentration of hemoglobin in the blood of the female rats of the flight group was 9.8%, reliably below that of the vivarium and synchronous control groups. Concentration of reticulocytes in the blood of experimental animals was scarcely more than one quarter of that in the vivarium control and half that of the synchronous control (Table 6).

When the animals were examined several hours after reentry, the flight rats displayed a significant increase in the concentration of leukocytes in peripheral blood (Table 6) mainly attributable to increase in the number of neutrophils with segmented nuclei; the lymphocyte/neutrophil ratio decreased to 0.5, with the corresponding values being 2.1 in the synchronous group and 3.8 in the vivarium control. Such changes, representing an acute reaction to reentry of the spacecraft and return of the animals to Earth's gravity, have also been observed in previous experiments on biosatellites in male rats exposed to weightlessness for 18-22 days.

Animals in the flight group dissected on the day of reentry — day 18 of pregnancy — displayed a decrease in thymus weight to 238 mg, while the analogous weights were 338 and 273 mg for the vivarium and synchronous control groups, respectively ($p<0.05$). An analogous pattern was observed when the total number of lymphocytes in the thymus was counted: in the experimental condition there were 738 million, while there were 1149 million in the vivarium and 1044 million in the synchronous control group.

The weight of the adrenal glands in rats of the flight group was elevated to 92.8 mg, adrenal weight was 82.3 g in the vivarium, and 79.8 mg in the synchronous control group; however, the difference between the groups was not statistically significant ($p>0/05$).

The experimental animals displayed a reliable decrease in weight of the liver and myocardium (Table 7); the absolute weight of the kidneys in females of all groups was the same, but since the rats of the experimental group showed virtually no weight increase, the relative weight of

the rats of the experimental group showed virtually no weight increase, the relative weight of the kidneys was greater in the experimental than in the control animals ($p<0.02$) at the end of the experiment.

Table 6: Blood profile in peripheral blood of pregnant female rats several hours after space flight

Grp	n	Hemoglobin, g%	Reticulocytes, %	Leukocytes, thous/mm^3	Lymphocytes / Neutrophils
F	9	9.8±0.3 $p_{V,S}<0.001$	47.7±6.6 $p_{V,S}<0.001$	30.8±1.66 $p_{V,S}<0.001$	0.5±0.05 $p_V<0.002$ $p_S<0.001$
SC	10	13.4±0.4	116.1±9.0 $p_V<0.002$	9.7±0.62 $p_V<0/01$	2.1±0.3
VC	10	12.9±0.4	211.9±21.3	13.8±1.3	3.8±1.08

Table 7: Body and organ weight of female rats dissected on day 18 of pregnancy

Grp	n	Body weight	Organ weights, g				
			Thymus	Adrenals	Myocardium	Liver	Kidneys
F	5	293±6.5 $p_{V,S}<0.002$	0.238±0.028 $p_V<0.05$	0.0930±0.0035	0.676±0.012 $p_V<0.05$	10.3±0.65 $p_V<0.01$ $p_S<0.001$	1.86±0.07
SC	5	355±5.9	0.273±0.008 $p_V<0.05$	0.0798±0.0053	—	14.6±0.53	1.94±0.06
VC	5	349±11	0.338±0.026	0.0823±0.0033	0.778±0.027	13.3±0.05	1.93±0.07

P1043(23/89)Yurchovichova Ya, Yezhova D, Vigash M (Czechoslovakia), Serova LV (USSR.)
State of female rats exposed to weightlessness during pregnancy: Concentration of hormones in blood plasma.
In: Gazenko OG (editor).
Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness]***
Moscow: Nauka: 1988. Pages: 39-42.

Developmental Biology; Reproductive System; Endocrinology; STH, Prolactin, Corticosterone, Insulin
Rats; Female; Pregnant
Space Flight; COSMOS-1514

Abstract: It is well known that weightlessness affect neuroendocrine regulation in adult animals and, in addition, that space flight lasting approximately 3 weeks acts as a stressor of moderate intensity on male rats. Pregnancy alters certain endocrine functions and sensitivity to the environment. The most likely of these functions to respond to stress during pregnancy are the somatropic, lactotropic, and adrenocorticotropic.

Secretion of the hormones named is very sensitive to any stressor, with corticosterone and prolactin increasing rapidly. The level of growth hormone in rats decreases in response to stress as a result of intensified secretion of somatostatin, while secretion of insulin also decreases. For this reason it was of unquestioned interest to determine the level of these hormones in female rats exposed to weightlessness on COSMOS-1514 on days 13-18 of pregnancy.

Blood for analysis was taken when the animals were decapitated several hours after flight. Prolactin and somatotropic hormone were determined through radioimmune assay using specific antibodies or activated charcoal for separating the free and bound forms of the hormone. Hormone preparations and antiserum were provided by NIH MDDK (Bethesda, U.S.A.). Corticosterone was measured using a protein binding method. Insulin was measured through radioimmunoassay using a kit produced by the firm RIA OPIDI (Poland).

The female rats of the flight group did not manifest any reliable changes in level of growth hormone in plasma (Figure 6). However, it is noteworthy that the individual variability in this parameter was significantly less in the experimental group than in the control ($p<0.001$), which may be the result of the disappearance of rhythmic fluctuations in secretion of STH in the flight animals as a consequence of disruption of coordination between somatoliberin and somatostatin.

When concentration of corticosterone was measured in plasma in the rats of all three groups — flight and synchronous and vivarium controls — no reliable differences were found (Figure 6). The level of prolactin in experimental animals was reliably higher than in both control groups (cf. Figure 6). The reason for the elevated level of prolactin in pregnant rats of the flight groups may be summation of the effects of moderate stress and circulating estrogens. It is well known that on day 18 of pregnancy rats' levels of estrogen are very high. Estrogens increase sensitivity to lactotropic impulses. This is probably the reason why space flight factors, which did not affect the levels of growth hormones or corticosterone, had a marked effect on prolactin.

Concentration of insulin in blood plasma of rats of the flight group was not significantly different from that in the vivarium control. In the synchronous control group the level of insulin was reliably higher than in the vivarium control and flight groups. The concentration of glucose in the plasma of experimental animals was reliably lower than in both controls (Figure 7).

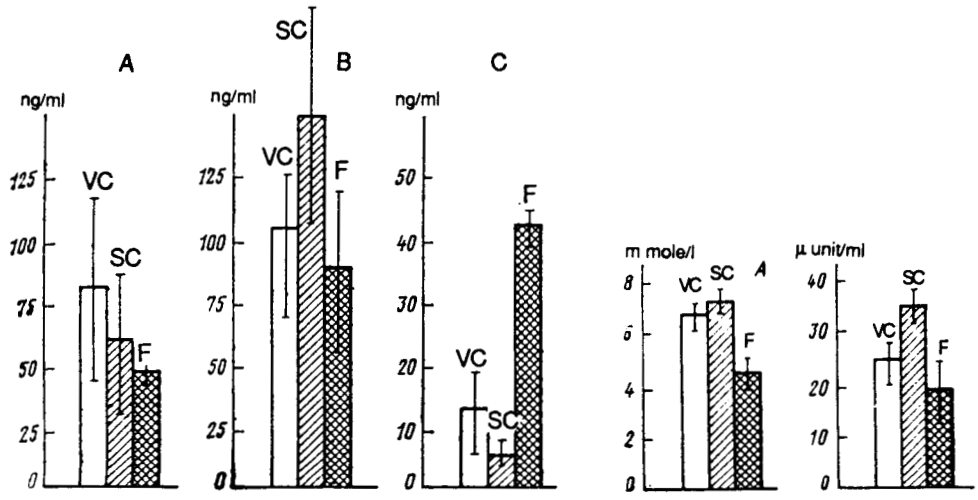


Figure 6: Concentration of somatotropic hormone (A), corticosterone (b) and prolactin (C) in the blood of female rats

Figure 7: Concentration of glucose (A) and insulin (B) in the plasma of female rats

P1044(23/89) Kvetnyanski R, Blazhichek P, Makho L (Czechoslovakia), Serova LV (USSR).
State of female rats exposed to weightlessness during pregnancy:The sympathetic adrenal system.
In: Gazenko OG (editor).
Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages: 42-43..

Developmental Biology; Reproductive System; Endocrinology, Sympathetic Adrenal System
Rats; Female; Pregnant
Space Flight; COSMOS-1514

Abstract: The status of the sympathetic adrenal system of female rats flown on COSMOS-1514 during days 13-18 of pregnancy was evaluated on the basis of concentrations of catecholamines in blood plasma and adrenal glands and the activity of their metabolic enzymes in the adrenal gland. Adrenaline, noradrenaline and dopamine were determined using Peuler and Johnson's method, activity of tyrosine-hydroxylases was measured using Nagatsu's method, and activity of phenylethanolamine-N-methyltransferase, was measured using Axelrod's method. The results obtained are presented in Figure 8.

A reliable decrease occurred in concentration of adrenaline in the adrenal glands of the flight animals compared to the synchronous and vivarium controls, while concentrations of noradrenaline and dopamine were unaltered. The activity of tyrosine-hydroxylase — the key enzyme of catecholamine synthesis — was elevated in the experimental group, while activity of phenylethanolamine-N-methyltransferase was the same as the control. There were no reliable changes in concentrations of adrenaline and noradrenaline in the blood of flight animals.

It should be noted that changes in metabolism of catecholamines discovered in pregnant female rats after a 5-day space flight were significantly greater than the changes observed in males after flights on COSMOS-936 and COSMOS 1129 lasting about 3 weeks, and also after a 7-day flight of males on COSMOS-1667. This suggests a greater stress reaction in the female rats exposed to weightlessness during pregnancy.

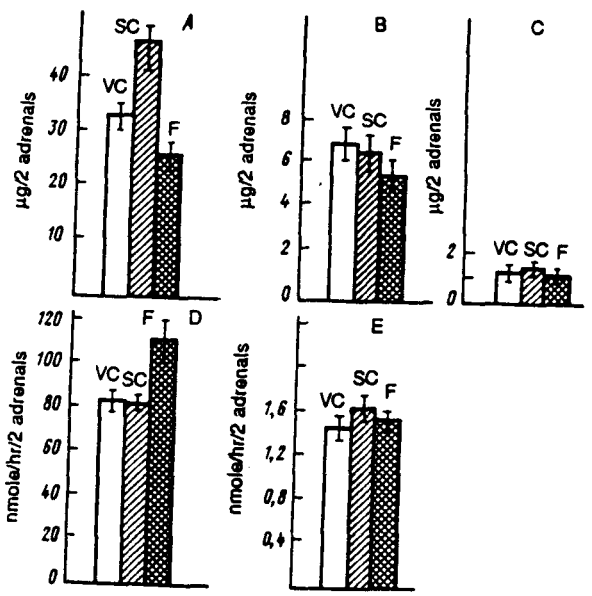


Figure 8: Concentration of adrenaline (A), noradrenaline (B), dopamine (C), activity of tyrosine-hydroxylase (D) and phenylethanolamine-N-methyltransferase (E) in the adrenal glands of female rats

P1045(23/89) Knopp Ya, Brtko Ya. (Czechoslovakia), Serova LV (USSR)
State of female rats exposed to weightlessness during pregnancy: The thyroid gland.
In: Gazenko OG (editor).
Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages: 43-44.

Developmental Biology; Reproductive System; Endocrinology, Thyroid
Rats; Female; Pregnant
Space Flight; COSMOS-1514

Abstract: The state of the thyroid gland of animals exposed to weightlessness during pregnancy was evaluated on the basis of the concentration of the major hormones, thyroxin and triiodothyronine, in thyroid tissue.

The tissue of the thyroid gland was homogenized in a buffer solution (0.04 M tromethamine; 0.11 M NaCl; 0.001 M 2-mercapto-l methyl-imidazole, pH 8.4, 0.25 ml per gland). Complete hydrolysis of the tissue was attained by using the enzyme pronase (2 mg in 50 µl buffer solution and 0.4 ml homogenate). One drop of toluene was added to the mixture, which was stirred constantly during incubation for 16 hours at 37°. After completion of hydrolysis, the samples were added to a buffer solution and the concentrations of thyroxin and triiodothyronine were determined using radioimmunoassay. (Concentrations of hormones were computed per 1 mg protein, determined using Lowry's method.

The results obtained are presented in Table 8, which shows the absence of changes in the state of the thyroid gland in animals exposed to weightlessness: concentrations of triiodothyronine and thyroxin in thyroid tissue were identical in the experimental animals and those of the vivarium control. In the synchronous control group, both parameters were reliably depressed.

Table 8: Concentrations of triiodothyronine and thyroxin in hydrolysates of the thyroid glands of female rats, µk/ng protein

Groups	n	Triiodothyronine	Thyroxin
F	5	0.50±0.12	1.50±0.42
SC	5	0.11±0.02	0.21±0.009
VC	6	0.35±0.07	1.40±0.33

P1046(23/89) Vacek A, Bartanichkova A, Rotkovska D (Czechoslovakia), Michurina TV, Domaratsskaya YeS, Serova LV (USSR)
State of female rats exposed to weightlessness during pregnancy: Hemopoietic stem cells.
In: Gazenko OG (editor).
Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages: 44-45.

Developmental Biology; Reproductive System; Hematology, Hemopoietic Stem Cells
Rats; Female; Pregnant
Space Flight; COSMOS-1514

Abstract: Hemopoietic stem cells are a sensitive target which reacts to the effects of a variety of chemical and physical factors. Changes in the size of the stem cell pool in bone marrow have been described in rats after exposure to hypergravity and weightlessness.

This work investigated the effects of weightlessness on the quantity and distribution of hemopoietic cells (CFUs) in female rats exposed to weightlessness during days 13 to 18 of pregnancy. Bone marrow (from the femur) and the spleens from experimental animals were homogenized in an M 199 medium and injected intravenously into recipient rats (aged 21-28 days), irradiated in a dose of 9.0 Gy 2 hours before the transplant. The numbers of cells in a suspension was counted in a Goryayev chamber; depending on the number of cells in individual groups, 15-20 recipients were used, each of which had been injected with 2×10^7 spleen cells or 2×10^6 bone marrow cells. On day 11 after transplant of the hemopoietic tissue, the spleen was removed from the recipients and fixed in a Charnow solution and macroscopically discernable cell colonies were counted on its parietal surface.

The total number of karyocytes in the bone marrow of flight animals was lower than in the vivarium control, but did not differ from the synchronous control At the same time, the concentration of CFUs was significantly lower in flight animals than in members of either control group, and as a result, the total number of CFUS in the bone marrow of the femur was lower in experimental rats (Figure 9).

The total number of splenocytes in the spleens of experimental rats was also reliably lower than that of the vivarium control group, but did not differ from the synchronous control. The concentration of CFUS (per 10^6 splenocytes) was virtually identical in the experimental and control groups, while the total number of CFUs was lower in the spleens of flight and synchronous control animals than in the vivarium group (Figure 9).

Thus, exposure of pregnant female animals to weightlessness for 5 days was accompanied by a significant decrease in the concentration and total number of CFUs in bone marrow. The data obtained are consistent with results obtained previously in examinations of male rats after space flights of greater duration and demonstrate that even exposure to weightlessness for as little as 5 days can alter the quantity of CFUs. The reason for such changes may be migration of CFUs from bone marrow, their death, or decrease in the number of the hemopoietic cells that generate them.

The total number of CFUs in the spleens of animals exposed to space during pregnancy was also depressed, but an analogous decrease was noted in the synchronous control group.

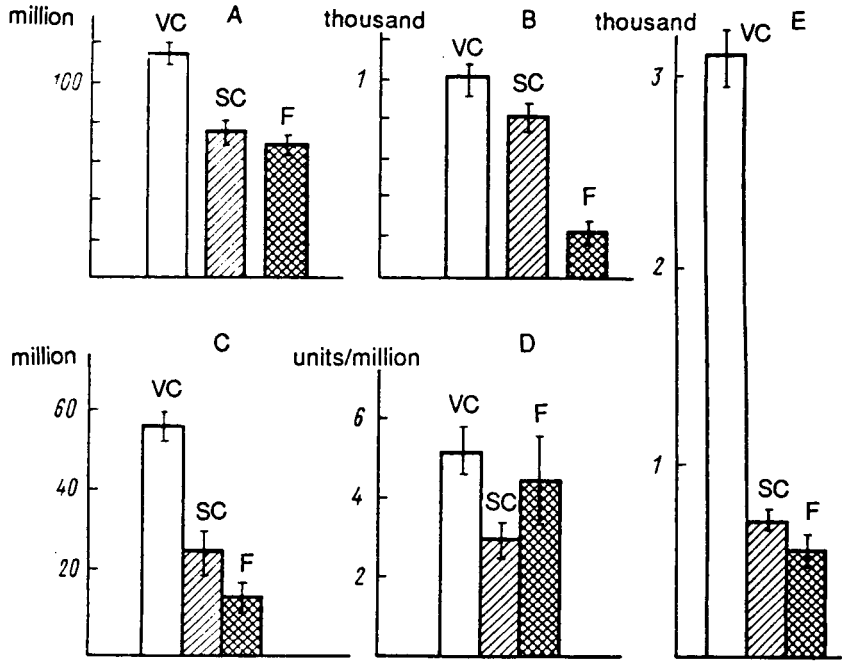


Figure 9. Characteristics of bone marrow and spleens of female rats, total number of karyocytes (A), CFUs (B) in bone marrow; total number of splenocytes (C) and concentrations (D); and total number of CFUs (E) in the spleen.

P1047(23/89) Denisova LA, Lavrova YeA, Natochin YuV, Serova LV, Shakhmatova Yel. (USSR)
State of female rats exposed to weightlessness during pregnancy: Concentrations of fluids and electrolytes in tissues.
In: Gazenko OG (editor).
Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages: 45-47.

Developmental Biology; Reproductive System; Body Fluids, Fluid-Electrolyte Concentrations
Rats; Female; Pregnant
Space Flight; COSMOS-1514

Abstract To study fluid-electrolyte composition in tissues of animals exposed to weightlessness during pregnancy, experimenters determined the concentrations of fluid, sodium, potassium, calcium, and magnesium in the liver, kidney, skin, and bone tissue (tibia). The tissues were weighed, placed on quartz glass, and dried at 105° until a constant weight was reached. Then the samples were placed in quartz test tubes to which concentrated nitric acid was added and subjected to a dry-air bath at 80° C until the organic substance had dissolved completely, after which the acid was boiled off and the samples diluted with distilled water. Quantities of sodium and potassium was determined by flame photometry in an air-propane flame; calcium and magnesium were measured in an air-acetylene flame on a atomic adsorption spectrophotometer.

The concentration of fluid in the examined tissues of flight animals was the same as in the control. No reliable differences were noted in concentrations of potassium, sodium, or magnesium in the liver, kidney, skin, and bone tissue. However, the level of calcium in the liver and kidneys of the flight animals was depressed by almost a factor of two, the change in the level of calcium in the skin of animals of the flight group was less pronounced than in the liver and kidneys, while no reliable changes were found in the bone tissue (tibia) (Figure 10).

These results differ from results obtained from examination of male rats after a 7-day space flight on COSMOS-1667. Unlike females, the males showed no reliable changes in concentration of calcium in any of the organs studied.

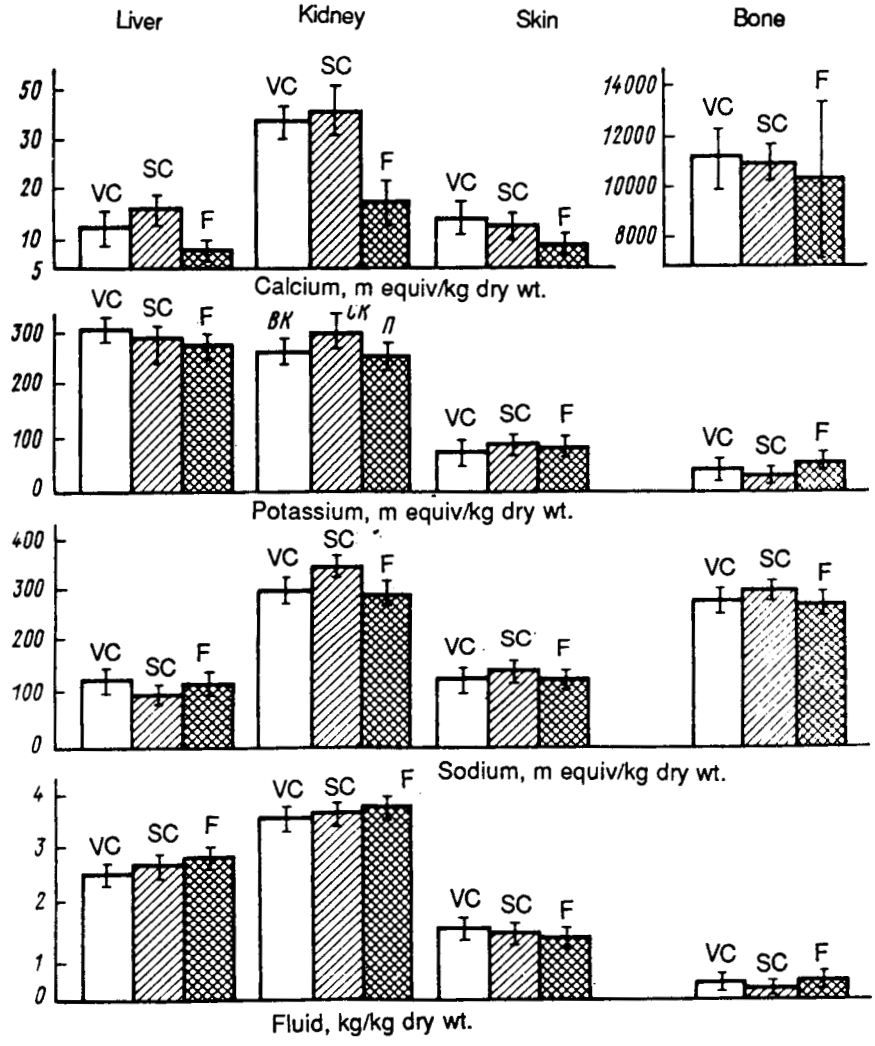


Figure 10: Levels of fluid and electrolytes in some tissues of pregnant rats exposed to space

P1048(23/89) Lyuderits P, Markvardt D, Vachtel Ye (GDR), Belakovskiy MS (USSR), Hecht K, Grosser I (GDR).
State of female rats exposed to weightlessness during pregnancy: Levels of electrolytes in the coats and tails of the animals.
In: Gazenko OG (editor).
Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages: 47-48.

Developmental Biology; Reproductive System; Body Fluids; Electrolytes; Coats, Tails
Rats; Female; Pregnant
Space Flight; COSMOS-1514

Abstract: The levels of calcium, magnesium, strontium, iron, phosphorus, zinc, copper, manganese, potassium, and sodium were measured in the coats of the animals exposed to space on the biosatellite, using an atomic-emission spectrometer with an inductively bound flame. Analysis was performed on samples of the coat (0.2-0.3 g) taken from the rats' backs and samples from the tip of the tail (ca. 1.5 g). The results obtained are presented in Table 9.

No reliable changes were noted in the tail tissues of flight animals with respect to levels of mineral elements in comparison with the synchronous control group. The coats of the experimental animals showed a reliable elevation in level of potassium, iron, phosphorus, copper, and manganese compared to both controls.

Table 9: Levels of mineral elements in the tails and coats of female rats

Group	Ca	Mg	Sr	Fe	P
		Tail, µg/g moist tissue			
F	34.1±1.07	597±16.02 $p_V<0.05$	16.7±1/12	36.1 ±3.07	15.4±0.55 $p_V<0.05$
SC	31.5±1.27	551±19.7	15.8±0.85	45.7±4.09	15.6±0.63 $p_V<0.05$
VC	32.6±0.6	553±9.9	16.3±0.44	45.5±2.65	13.6±0.31
		Coat µg/g dry weight			
F	521±83.88	161±23.04	0.76±0.13	96.3±11.63 $p_{V,S}<0.001$	3090±594.2 $p_{V,S}<0.01$
SC	375±53.7	119±14.37	0.51±0.07	25.3±1.25	435±23.35
VC	398±14.24	118±6.86	0.51±0.04	30.2±3.65	365±21.22

Group	Zn	Cu	Mn	K	Na
		Tail, µg/g moist tissue			
F	53.2±1.43	1.42±0.05 $p_V<0.01$ $p_S<0.05$	1.46±0.16 $p_V<0.01$	3.04±0.34 $p_V<0.01$	2.60±0.21 $p_V<0.05$
SC	50.1±0.63	1.38±0.06 $p_V<0.05$	2.71±0.38 $p_V<0.001$	3.30±0.36 $p_V<0.05$	2.97±0.25
VC	50.2±1.12	1.16±0.04	2.63±0.2	1.20±0.06	1.70±0.12
		Coat µg/g dry weight			
F	202±3.61	12.3±0.33 $p_V<0.01$	3.06±0.52 $p_{V,S}<0.0$	3170±652.1 $p_{V,S}<0.01$	2380±478.97
SC	206±1.84	11.1±0.5	1.41±0.22	776±86.76	2420±346.3
VC	211±8.5	11.0±0.2	1.55±0.23	531±38	2000±71.6

P1049(23/89) Ahlers I, Ahlersova E (Czechoslovakia). Serova L.V (USSR.), Toropila M (Czechoslovakia).
State of female rats exposed to weightlessness during pregnancy: Lipid Metabolism.
In: Gazenko OG (editor).
Ontogenez mlekopitayushchikh v nevesomosti *[Ontogeny of mammals in weightlessness.]*
Moscow: Nauka: 1988. Pages: 48.-49.

Developmental Biology; Reproductive System; Metabolism, Lipid
Rats; Female; Pregnant
Space Flight; COSMOS-1514

Abstract: It has previously been established that exposure of animals to weightlessness induces marked changes in the composition of tissue lipids. Since pregnancy can be considered a kind of functional stress on the body of the mother, and tissue lipids are one of the major sources of energy rapidly mobilized in response to a variety of environmental factors, evaluation of the state of tissue lipids in female rats exposed to weightlessness on COSMOS-1514 during days 13-18 of pregnancy was of unquestionable interest.

With this goal, on the day of reentry (day 18 of pregnancy) concentration of triglycerides in the liver and thymus, concentration of NEFA (non-esterified fatty acids) in white and brown fat tissue, concentration of cholesterol in the liver, and concentration of phospholipids in the liver and thymus were measured in the female rats.

The experimental group displayed an increase in the concentration of NEFA in white and brown fat tissue and an accumulation of triglycerides in the liver; concentrations of cholesterol and phospholipids were not altered in the liver. In the thymus of flight animals, there was a tendency for triglycerides to decrease and phospholipids to increase (Figure 11). The changes described were analogous to the pattern observed previously in male rats after longer duration space flights. The major changes — accumulation of NEFA in fat tissue and triglycerides in the liver — are indicative of the biochemical pattern of fatty liver.

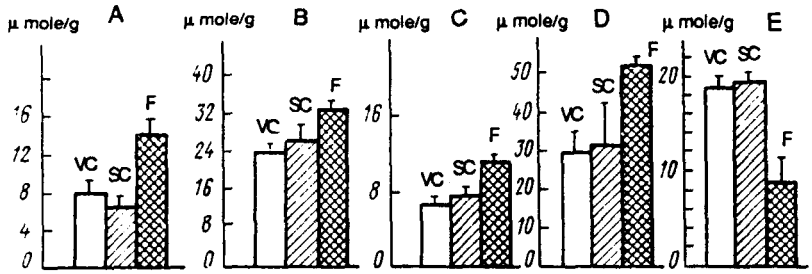


Figure 11. Lipid metabolism parameters in female rats: NEFA in white (A) and brown (B) fat; triglycerides in the liver (C); triglycerides (D) and phospholipids (E) in the thymus.

P1050(23/89) Mishurova E, Kropachova K, Gabor Ya (Czechoslovakia).
State of female rats exposed to weightlessness during pregnancy: Concentration of nucleic acids and polydeoxyribonucleotides in tissues.
In: Gazenko OG (editor).
Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages: 49-51.

Developmental Biology; Reproductive System; Genetics, Nucleic Acids, Polydeoxyribonucleotides
Rats; Female; Pregnant
Space Flight; COSMOS-1514

Abstract: Certain experimental treatments (e.g., irradiation, injection with cytostatic agents or glucocorticoids) induce decomposition of deoxyribonucleoproteins (DNP) in lymphatic and hemopoietic tissues. Decomposition of DNP is accompanied by elevation in the level of polydeoxyribonucleotides which are a mixture of oligonucleotides, and a decreased level of DNA. The level of polydeoxyribonucleotides is elevated for 2 to 18 hours, with the maximum rise occurring 6 hours after treatment. The increased level of polydeoxyribonucleotides is a good indicator that acute damage to the sensitive cells occurred a short time before the animals were studied. In the case of repeated exposure this reaction may be identified only after regeneration of sensitive cells (mainly lymphocytes and erythroblasts), i.e. approximately 7 days after the first treatment.

Experiments on male rats exposed to weightlessness for approximately 3 weeks and studied several hours after reentry, revealed a decrease in concentration of nucleic acids in the spleen and thymus, and an increase in the level of polydeoxyribonucleotides, attesting to damage to DNP during the landing phase of the biosatellite. The experiment on COSMOS-1514 involved an analogous study of pregnant female rats. This experiment measured the concentration of nucleic acids in the liver, spleen, thymus and blood leukocytes using a modification of the method developed by Tsaneva and Markova and also estimated the decomposition of DNP on the basis of levels of polydeoxyribonucleotides. The most pronounced changes were found in the spleen. In the flight group, the concentrations of nucleic acids were within normal limits, but due to the decreased weight of the organ, the total levels of RNA and DNA decreased compared to the vivarium control group by virtually a factor of two. In the synchronous control group the decrease in concentration of nucleic acids was more moderate (Figures 12, 13). The level of polydeoxyribonucleotides in the spleen of the animals of the flight group was the same as in the vivarium control and higher than in the synchronous control, where levels of this parameter were very low (Figure 14).

Concentrations of DNA and RNA in thymus tissue of female rats of the flight group did not differ significantly from control values (Figures 12, 13). At the same time the total amount of nucleic acids in the organ was lower in the experimental than in the vivarium control group. For DNA, the analogous changes were also observed in the synchronous control group. The level of polydeoxyribonucleotides in thymus tissue was depressed to an equal extent in the flight and synchronous control groups (Figure 14).

In blood sediment of pregnant rats of the flight group, the concentration of DNA was within control limits, while the concentration of RNA decreased in comparison to the vivarium control by approximately one half. Decreases in RNA concentration were less substantial in the synchronous control group (Figures 12, 13). It can be concluded that the decreased concentration of RNA in blood sediment is mainly a consequence of the lower admixture of reticulocytes; the quantity in the flight group was half as much as in the synchronous control and one third that of the vivarium control (Cf. Table 6),

The livers of female flight rats showed no changes in the concentration and total amounts of DNA compared with both control groups (Figure 13). The concentration of RNA was somewhat elevated, while the total amount in the organ was depressed due to decrease in liver mass (Figure 12). The concentration of polydeoxyribonucleotides was unaltered (Figure 14).

The changes described above in concentrations of nucleic acids in the tissues of pregnant female rats after a 5-day space flight correspond to data obtained from the study of male rats after longer duration space flights of biosatellites. In the spleens of the males, the level of RNA was depressed by 25-45%, while in the pregnant females from COSMOS-1514, it was depressed by 50%; level of DNA was depressed by 30-50% in males and 59% in females. In the thymus, RNA level was depressed 0-40% in the males and 40% in pregnant females, while DNA was depressed 0-33% in males and 36% in females. When these figures are compared, it is evident that the decrease in nucleic acids in pregnant females after a 5-day flight is at the lower end of the spectrum for the males after flights of approximately 20 days. The differences obtained may be considered either an indication of the higher sensitivity of pregnant females to space flight conditions or as one of the indirect demonstrations of damage inflicted upon sensitive cells during spacecraft launch and the animals' transition to weightlessness. The second hypothesis was confirmed by the absence of signs of decomposition of DNA in the spleen and thymus of animals after a short-term flight on COSMOS-1514. Low polydeoxyribonucleotides levels and the lack of capacity for a second response to repeated stimulation (during reentry) is typical of the stage preceding regeneration of sensitive cells After a longer exposure to weightlessness, sensitive cells, damaged at launch evidently regenerated, and for this reason decomposition of DNA induced by transition between weightlessness and hypergravity is manifest as an increase in the level of polydeoxyribonucleotides several hours after completion of a 20-day flight.

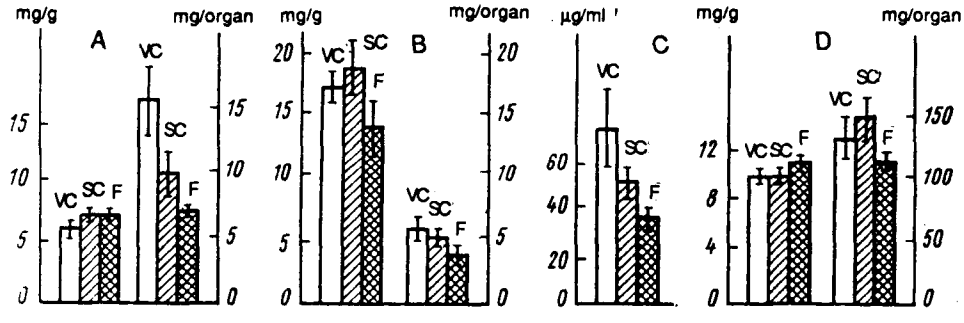


Figure 12: Concentration of RNA in organs of female rats: spleen (a0, thymus (b),. blood sediment (C), liver (d)

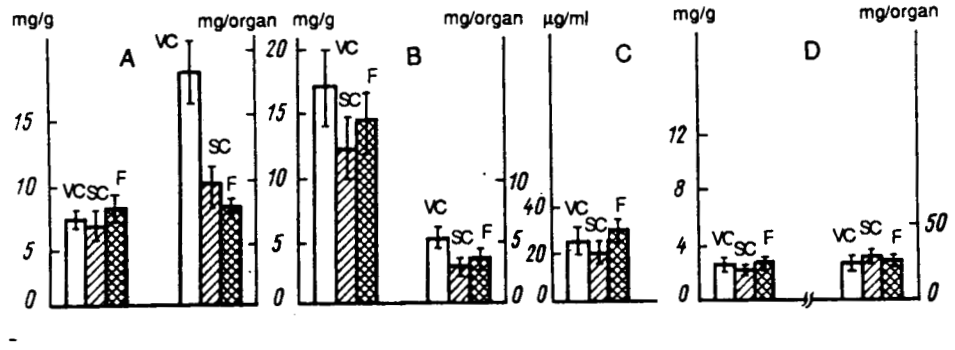


Figure 13: Concentration of DNA in organs of female rats: spleen (a), thymus (b), blood sediment (c), liver (d)

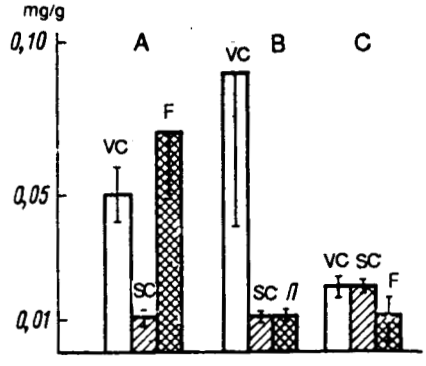


Figure 14: Concentration ofpolydeoxyribonucleotides in the : spleen (a), thymus (b), blood sediment (c), liver (d)

P1051(23/89) Makeyeva VF, Kosmoslova GS, Yegorov IA (USSR).
State of female rats exposed to weightlessness during pregnancy: Biosynthesis of nucleic acids.
In: Gazenko OG (editor).
Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages: 51-53.

Developmental Biology; Reproductive System; Genetics; Nucleic Acids; Biosynthesis; Enzymology
Rats; Female; Pregnant
Space Flight; COSMOS-1514

Abstract: In 10 experiments with male rats on COSMOS biosatellites, both acute and chronic reactions to space flight factors were identified in the genetic system of the cells of the liver and lymphoid organs The present research attempted to identify the characteristics of such reactions in female rats, exposed to space on COSMOS-1514 on days 13-18 of pregnancy.

RNA-synthesizing activity was determined in the nuclei of the liver, and rate of DNA and RNA biosynthesis in lymphocytes of the spleen. Concentrations of nucleic acids and protein were measured in liver tissue. To study RNA-synthesizing activity in liver tissue, the nuclei were isolated in a solution of dense sucrose. A portion of the nuclei was used to determine transcription, and a solubilized RNA-polymerase enzyme was obtained from the remainder. Conclusions were drawn concerning enzyme activity and RNA synthesis in the nuclei on the basis of inclusion of a radioactive precursor, ^{3}H-UMP, in acid-insoluble products of RNA-polymerase reactions. Rates of RNA and DNA biosynthesis in spleen lymphocytes were determined on the basis of *in situ* inclusion of radioactive precursors. Amounts of nucleic acids were measured spectrophotometrically using a method developed by Blobel and Potter, and quantities of protein were measured according to Lowry.

Figure 15 presents data indicative of the endogenous synthesis of RNA in liver nuclei of rats on the day of reentry (day 18 of pregnancy). These data suggest that after flight, transcription activity had increased compared with the vivarium control by almost a factor of two. In the synchronous condition, RNA synthesis in nuclei also increased, but to a lesser degree (30%) than in rats of the flight group.

It is well known that RNA synthesis in the cell depends to a significant extent on activity of RNA polymerases, enzymes that synthesize various types of RNA on the DNA matrix. Investigation of activity of solubilized RNA-polymerases synthesized from liver nuclei showed that in pregnant rats in the flight and synchronous conditions, the changes are similar to those noted with regard to RNA synthesis in the nuclei; i.e., after space flight, enzyme activity exceeded control levels by a factor of two, while in the synchronous conditions it was elevated by 37%. The positive correlation between rate of RNA synthesis and activity of RNA-polymerases in the nuclei of hepatocytes may support the dominant role of enzymatic components in the transcription changes observed.

Results of quantitative measurement of nucleic acids in liver tissue (Table 10) are also consistent with these data. Animals of the flight group showed an elevated level of RNA. It should be noted that in the preceding experiments performed on male rats, the opposite response was observed — decreased concentrations of RNA. Evidently, the slight increase in RNA in this experiment is associated with the development of compensatory reactions in pregnant rats in response to the extreme conditions of space flight.

Table 11 presents results of investigations of the rate of inclusion of radioactive precursors ^{3}H-thymidine in DNA and ^{14}C-uridine in RNA lymphocytes of the spleen. After space flight, synthesis of both DNA and of RNA altered in pregnant rats. However, it is clear that these changes are not of the same nature. DNA replication was depressed compared to the vivarium control by almost a half, while at the same time RNA synthesis accelerated. There were no significant changes in these parameters in animals of the synchronous control group. These data suggest that changes in the metabolism of nucleic acids in spleen lymphocytes of the experimental animals were due to the effects of weightlessness and not to concomitant space flight factors. Decreased DNA synthesis in spleen cells is most likely due to chronic stress developing in flight due to decreased loading of the musculoskeletal system. Indeed, as was demonstrated earlier, depression of DNA replication in spleen cells also manifests itself relatively clearly in male rats both after space flights, and in simulation experiments involving long-term hypokinesia, although, RNA as well as DNA synthesis was depressed.

Activation of RNA synthesis was a response peculiar to spleen lymphocytes of pregnant flight rats. In this case evidently there is no functional link between the changes in rate of transcription and the rate of renewal of the DNA matrix. At the same time, one might postulate acceleration of RNA synthesis with segments of the genome responsible for synthesis of proteins important for the formation of adaptive reactions. It has not been ruled out that some role is played here by the increased formation of stable ribosomes of RNA. This hypothesis is partially corroborated by the increase in the RNA/DNA ratio in lymphocytes, from 0.52±0.01 in the vivarium control to 1.42±0.11 in the experimental group.

Evidently, the changes in metabolism in RNA lymphocytes of the spleen identified in pregnant animals in the flight group serves to activate the trophic function of the immune system. This may facilitate support of the defensive potential of the mother's body, which is extremely important for normal pregnancy.

Table 10: Concentration of nucleic acids and proteins in the liver, mg/g moist tissue

Group	DNA	RNA	RNA/DNA	Protein
F	3.3±0.17	15.3±0.60	4.6	154±7
SC	2.8±0.20	13.4±0.50	4.8	155±9
VC	3.4±0.18	13.8±0.45	4.1	150±7

Table 11: Rate of inclusion of radioactive precursors in DNA and RNA of spleen lymphocytes

Group	^{3}H-thymidine, imp/min, µg DNA	^{14}C-uridine, imp/min, µg RNA
F	81.9±2.8	15.6±0.7
SC	119.3±10.2	10.0±1.6
VC	141.0±2.0	10.4±0.9

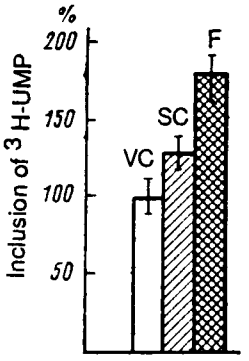


Figure 15: Endogenous synthesis of RNA in liver nuclei

P1052(23/89) Hemet Sh. (Czechoslovakia)
State of female rats exposed to weightlessness during pregnancy: Activity of certain enzymes in the liver.
In: Gazenko OG (editor).
Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages: 54

Developmental Biology; Reproductive System; Enzymology, Liver Enzymes
Rats; Female; Pregnant
Space Flight; .COSMOS-1514

Abstract: Previous biosatellite experiments utilized measurement of the activity of a number of liver enzymes, along with other parameters, to indicate the presence of stress in animal subjects One sign of acute stress is elevated activity of tyrosine aminotransferase (TAT) and tryptophan pyrrolase (TP), while a sign of chronic stress is elevated activity of alanine-aminotransferase (ALT) and aspartate-aminotransferase (ST). In the current experiment analogous investigations were performed on pregnant rats exposed to space on COSMOS-1514 on days 13-18 of pregnancy. Methods used are not described here. The results obtained are presented in Table 12. Enzyme activity is given per 1 g protein in the homogenate.

No reliable differences were found between the subjects exposed to weightlessness during pregnancy and control animals in activity of TAT, TP, ALT, and ST. These results are not consistent with material obtained earlier from examination of male rats, in which activity of these liver enzymes was elevated after space flight. It should be noted that other signs of acute and chronic stress were as high (neutrophilia, lymphopenia, etc.) or higher (retarded weight gain, changes in catecholamine metabolism) in pregnant rats exposed to space as in the previously studied males.

Table 12: Activity of certain enzymes in the livers of pregnant female rats

Group	TAT, mmole g/min	TP, mmole/g/hr	ALT, mmole/g/min	AST, mmole/g/min
F	21.7±10.1	17.2±6.5	54.6±26.9	273±47
SC	36.9±7.2	9.9±2. 6	48.6±25.7	279±11
VC	21.5±8.6	15.4±7.5	30.0±12.9	253±23

P1053(23/89) Oshadal B, Peloukh V, Kolar F, Rikhter Z, Dragota Z (Czechoslovakia)
State of female rats exposed to weightlessness during pregnancy: State of the myocardium.
In: Gazenko OG (editor).
Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages: 54-55.
Developmental Biology; Reproductive System; Cardiovascular and Respiratory Systems, Myocardium
Rats; Female; Pregnant

Abstract: Female rats exposed to space on COSMOS-1514 on days 13-18 of pregnancy were dissected on the day of reentry. The heart muscle was frozen in liquid nitrogen and stored in dry ice until used in the experiment. After it was thawed, the weight of the myocardial ventricles and the septum were measured, along with their fluid content (by drying to a constant weight at 80°), concentration of glycogen and protein, and also activity of ATP-ase myosin.

In flight animals there was a reliable decrease in total myocardial weight attributable to a 19% decrease in the weight of the septum, a 15% decrease in the weight of the right ventricle ($p<0.05$), and a non-significant 9.5% decrease in the weight of the left ventricle.

The concentration of fluid in myocardial tissue (per unit dry weight), and also the concentrations of protein and glycogen in the experimental and vivarium control conditions, were identical. There were no reliable intergroup differences found in activity of myocardial ATP-ase. Unfortunately, the analogous parameters were not measured in synchronous animals, and thus the flight group was compared only to the vivarium control.

P1054(23/89) Pospichilova I, Pospichil M (Czechoslovakia), Serova LV (USSR.)
State of female rats exposed to weightlessness during pregnancy: Collagen metabolism in the skin and bone tissue.
In: Gazenko OG (editor).
Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages: 55-56

Developmental Biology; Reproductive System; Metabolism; Collagen; Musculoskeletal System, Bone Tissue
Rats; Female; Pregnant
Space Flight; COSMOS-1514

Abstract: It is well known that weightlessness induces marked changes in the musculoskeletal system. Animals previously exposed to space on COSMOS biosatellites displayed changes in the structure and metabolism of bone tissue, along with decreased strength of bones of the limbs and vertebrae. It thus appeared to be of interest to study the effects of weightlessness on collagen metabolism, which to a significant degree determines the biomechanical (support) functions of connective tissue, in females rats exposed to space during pregnancy. Bone tissue (femur) and skin, consisting of 50 and 40% collagen, respectively, were selected for study.

Skin (without the hair) was taken for analysis from the back of the animal: the femur was cleaned of bone marrow. Bone samples were frozen in liquid nitrogen and mechanically homogenized, and solubilized in 0.5 M acetic acid in the presence of Behringer pepsin (three times in 24 hours, 100 mg pepsin per 1 gram tissue at 4°) and then processed according to Ehrlich (1979) by the method of zonal precipitation chromatography using the FRAG-300 (France, Switzerland) programmed fraction collector. Hydroxyproline was measured in individual chromatographic peaks, and total protein in the glycoprotein peak. The total amount of insoluble collagen obtained using ultracentrifugation with solubilization of the samples was estimated on the basis of quantity of hydroxyproline and used to compute the proportion of soluble collagen.

Amount of soluble collagen in bone tissue samples was measured in precisely the same way. Insoluble collagen was processed with cyanogen bromide. Collagen protein was separated out using peptides specific to collagen types I and III. The peptides, which were freed using cyanogen bromide, were divided on ionex systems of "rapid fluid chromatography" using a completely automated system. Their molecular weight was measured using permeation chromatography under pressure. The ratios of peptides with varying molecular weights were used to determine the ratio of the different types of collagen.

Analysis of the skin of flight animals, sacrificed several hours after a 5-day space flight, revealed significant changes in parameters of pepsin-soluble collagen metabolism compared to control rats. No differences were found between the vivarium and synchronous control, and for this reason their results are combined (Table 13).

Flight animals displayed a 22% elevation of the level of soluble collagen in skin compared to the control ($p<0.01$), the ratio of hydroxyproline (i.e., collagen) to glycoproteins in the experimental group was depressed by more than a factor of 20 mainly due to the increase in glycoproteins. When various types of collagen were measured in the skin of the experimental animals, it was observed that the proportion of type I collagen decreased slightly and the proportion of type III collagen increased a great deal (Table 13). These results indicate that metabolic activation of connective tissue has occurred. The changes found in the analysis of soluble collagen in the skin of flight rats are characteristic of the skin of young, growing animals.

Analysis of soluble collagen of bone tissue in animals of the flight group, revealed no reliable differences in the ratios of different types of collagen. In the experimental group percentage of type I collagen was 21% compared to 14% in the control groups ($p>0.05$); type II collagen amounted to 2% and 1% in the experimental and control groups respectively; and type II collage was 9 and 11% ($P>0.05$). At the same time, analysis of pepsin-insoluble collagen in bone revealed substantial differences between the flight and control rats. The bones of animals in the control groups contained only type I collagen, which is congruent with data in the literature. At the same time samples of bone tissues obtained from experimental rats showed a decrease in type I collagen and the appearance of type II collagen in a proportion of 35%. The decrease in type I collagen may be associated with an increase in the activity of collagenolytic enzymes, such as collagenase, catepsin and elastase. This hypothesis is supported by the increased number of catabolic peptides in soluble collagen of bone tissue in animals of the flight group, which reached a level of 47%, compared to a control group value of 28% ($p<0.05$) The presence of type III collagen in the bones of animals of the flight group is an interesting fact. In normal conditions this substance is produced by the smooth muscles, fibroblasts, and reticular cells, but not by osteoblasts. In the past it has not been found in bone tissue, with the exception of the inherited disturbances in connective tissue — *osteogenesis imperfecta* .

Table 13: Parameters of collagen metabolism in the skin of animals exposed to space flight during pregnancy

Group	Soluble collagen, %	Hydroxyproline, mg Glycorproteins, mg	Collagen type I, %	Collagen type III, %
F	83.7±2.7	25.7±1.6	93.88±0.89	6.12±0.89
	p<0.01	p<0.01	p<0.05	p<0.05
SC+VC	61.7±2.2	544.2±47.8	98.60±0.26	1.40±0.26

P1055(23/89) Oganov VS, Bakulin AV, Il'yin YeA, Lebedev VI, Stupakov GP (USSR), Shapper D, Alexander K, Frey I, Vico L, Nogues C (France).
State of female rats exposed to weightlessness during pregnancy: Structure and mechanical properties of bone tissue.
In: Gazenko OG (editor).
Ontogenez mlekopitayushchikh v nevesomosti ***[Ontogeny of mammals in weightlessness.]***
Moscow: Nauka: 1988. Pages: 56-60.

Developmental Biology; Reproductive System; Musculoskeletal System, Bone Tissue
Rats; Female; Pregnant
Space Flight; COSMOS-1514

Abstract: Bone research performed on female rats exposed to space on COSMOS-1514 during days 13-18 of pregnancy included evaluation of the density of bone composition; study of the number and activity of the major cellular elements in bone tissue; and evaluation of overall parameters of mineralization, the composition of the organic matrix and the mineral component, and biomechanical properties. The femur, tibia, and humerus bones and the thoracic and lumbar vertebrae were studied.

The methodology for processing the preparations and performing measurements is not described in detail here. Measurements made in the femur included: distance between two periosts in the middle third of the diaphysis, total thickness of the cortical layer (internal and external), and the mean diameter of the marrow cavity. In the proximal epiphysis of the tibia, experimenters measured the volume of trabecular bone tissue, which was considered to be the portion of the spongiosa tissue occupied by trabeculae in an area 0.8 mm in width below the growth cartilage (zone of new growth), and in the area another 0.8 mm lower (remodeling zone). In the zone of bone tissue modeling investigators measured the diameter of vertical cylinders — precursors of trabeculae, while in the zone of remodeling the mean diameters of trabeculae were measured. The mean thickness of the anterior and posterior cortices, their layers, and the volume of trabecular bone tissue were measured, and these values were used to compute the absolute volume of bone tissue, the volume of trabecular bone tissue and the ratios among them.

Activity of the cellular elements of bone tissue was evaluated using methods not described. Mean thickness of the growth plate in trabecular bone tissue in the thoracic and lumbar vertebrae, proximal epiphysis of the tibia and diaphysis of the humerus were measured to serve as a reflection of osteoblast activity. Measurements were made in zones of neoformation and remodeling. Activity of osteoclasts was estimated on the basis of how many were contained in 1 mm^3 spongiosa, and in trabecular tissue by how many were contained in a 1 mm^2 surface area of trabecular bone tissue. Differentiation was also measured in zones of neoformation and remodeling in the cortical layer of the endosteum In the cortical layer of the endosteum of the tibia, the surface of active resorption was measured in zones of neoformation and remodeling.

Composition of the organic matrix was studied in bone samples from the forearm and tibia. The procedures for processing the preparations, hydrolysis and separation of amino acids are not described. This method is based on determination of the proportional composition of collagen amino acids: proline, hydroxyproline, and also alanine and glycine in samples of bone tissue. After separation and measurement of these amino acids, the ratios of hydroxyproline to proline and glycine to alanine were computed.

Study of the mechanical properties, mineralization, and chemical composition of the mineral components of spongy bone tissue were performed on the proximal epiphysis of the shoulder (humerus). The mechanical properties of bone tissues in response to compression tests were

studied using the Instron device. The compression strength, proportionality limit, maximum relative deformation for the proportionality limit, modulus of elasticity, and specific work of elastic deformation were computed. Mineral saturation of the bone, concentration of organic substance, coefficient of mineralization (ratio between mineral mass and mass of organic substance), porosity, and levels of calcium, phosphorus, magnesium, sodium, potassium, zinc, and silicon were measured. Amount of each element in one gram of ash and a unit volume of bone were obtained by computation, and then the concentration of the element in the mineral component was multiplied by the coefficient of mineralization to determine how much of the element was contained in a unit mass of organic bone matrix.

Study of osteoclast activity in flight animals revealed a tendency for the number of cells to increase in a unit volume of spongiosa tissue in the zone of neoformation and remodeling in the tibia bone and also in vertebral trabeculae. For the thoracic vertebrae the difference was statistically significant ($p<0.05$). An analogous tendency was observed in the number of osteoclasts in a unit volume of trabecular tissue. Analysis of variance revealed a statistically reliable increase in the surface occupied by osteoclasts in the metaphysial bone laminae (plate) of the humerus in flight animals compared to that of the synchronous control group. There was a tendency for the surface of the osteocytic lacuna to increase in the endocortical zone of the humeral diaphysis in the flight and synchronous groups compared to the vivarium control.

No intergroup differences were found in the thickness of osteoid tissue either in the zone of neoformation or the zone of remodeling in the tibia. The amount of osteoid in the thoracic and lumbar vertebrae was too small to be measured. The results of measurement of the width of osteoid tissue in the humeral diaphysis suggest a tendency for the periosteum to decrease in flight animals.

The ratio of trabecular bone tissue of the vertebrae to the overall volume of bone tissue and also the arrangement of trabeculae was the same in all three groups. It was shown that at the level of the tibial metaphysis the tubes of the primary spongiosa in the zone of neoformation and bone bands of the space below it (the remodeling zone) were comparable and had the same diameters. No changes were found in the volume of trabecular bone tissue, either in the tibia or in the vertebrae of animals in the three groups.

During the flight there were no significant changes in porosity of spongy bone tissue of the proximal epiphysis of the humerus. At the same time a substantial ($p<0.05$) decrease in the concentration of organic substance in the spongiosa of the proximal epiphysis of the humerus was found in the flight group compared with the synchronous control, evidently due to activation of resorption. The coefficient of mineralization of substance of the proximal epiphysis of the humerus was higher in experimental subjects than in control groups. The combined changes in the coefficient of mineralization of bone tissue and the concentration of organic substance increased mineral saturation in animals of the synchronous control. No significant differences were found in this parameter between rats of the flight and vivarium control groups.

Analysis of the organic matrix of the tibia and bones of the foreleg did not reveal any reliable differences between the experimental and control groups in the concentrations of hydroxyproline, proline, alanine, or glycine, which suggests the absence of changes in the overall content of collagen and its composition.

The 5-day space flight led to a decrease in the concentration of calcium in the mineral component of the proximal epiphysis of the humerus bone (Table 14). Concentration of calcium per unit mass of organic substance was also lower in the flight than in the control groups, suggesting decreased total concentration of calcium in bone, despite the increase in the coefficient of mineralization. The experimental animals displayed an increase in concentration

of phosphorus in bone tissue in the mineral as well as the organic substance of the bone (Table 14). As a result, the ratio of Ca/P was reliably lower in flight rats than in both control groups, which might indicate a relative decrease in the concentration of crystalline hydroxyapatite in the mineral component of bone. The concentration of potassium was identical in the bone tissue of animals of all three groups, while the concentration of sodium in flight rats was reliably higher than in the vivarium control, but did not differ from the synchronous control; the concentration of silicon in flight rats was depressed compared to the vivarium control, while the concentration of zinc was elevated. However, these differences were not statistically significant compared to the synchronous control (Table 14).

Study of the mechanical properties of the proximal epiphysis of humerus bones revealed a reliable decrease in the compression strength and maximum relative deformation in flight rats (Table 15). The modulus of elasticity of bone tissue showed a tendency to increase compared to both control groups, but these differences were not statistically significant. The results obtained confirm that it is possible for bone strength to decrease while its density remains unchanged under conditions of actual and simulated weightlessness, as had been established previously. Evidently this decrease is associated with a decrease in the concentration of calcium in the mineral component and the Ca/P ratio.

These results, taken together, support the conclusion that exposure of pregnant rats to weightlessness for 5 days is accompanied by an increase in the number of osteoclasts, and, evidently, activation of the processes of resorption of bone tissue, which, however, does not reach the stage of the main symptom of osteoporosis - loss of bone tissue.

Table 14: Levels of elements in bone tissue (proximal epiphysis of the humerus)

Group	Ca, mg	P, mg	Mg, mg	Na, mg
		Per 1 g ash		
F	387.4±4.55 $p_{V,S}<0.05$	127.7±2.42 $p_S<0.05$	8.37±0.325 $p_V<0.05$	10.14±0.63 $p_V<0.05$
SC	416.3±3.13	112.4±1.74	18.77±5.98	9.63±0.63
VC	415.2±3.7	115.2±8.85	35.25±3.63	7.22±0.68
		Per 1 g organic substance		
F	542.7±15.0 $p_S<0.05$	182.7±2.3 $p_{V,S}<0.05$	12.37±0.40 $p_V<0.05$	13.93±1.53 $p_V<0.05$
SC	574.6±2.94	155.8±4.98	19.47±6.65	13.43±1.10 $pv<0.05$
VC	566.5±12.08	154.7±12.13	45.94±4.94	10.45±0.377

Group	K, mg	Si, μg	Zn, μg	Ca/P
		Per 1 g ash		
F	1.503±0.229	46.56±2.02 $p_V<0.05$	771.5±45.21	3.04±0.091 $p_{V,S}<0.05$
SC	1.592±0.200	45.25±2.02 $p_V<0.05$	637.2±32.89	3.70±0.091
VC	0.813±0.44	92.39±10.52	565.3±51.47	3.73±0.098
		Per 1 g organic substance		
F	2.140±0.392	68.08±1.39 $p_V<0.05$	1135±115.5	
SC	2.186±0.337	60.61±2.98 $pv<0.05$	845±52.4	
VC	1.054±0.082	130.8±10.91	766±60.8	

Table 15: Mechanical properties of bone tissue (proximal epiphysis of the humerus)

Group	Proportionality limit, $N \cdot 10^{-1}/mm^2$	Compression strength, $N \cdot 10^{-1}/mm^2$	Maximal relative deformation	Modulus of elasticity. $N \cdot 10^{-1}/mm^2$	Specific work of elastic deformation $N \cdot 10^{-1} mm/mm^3$
F	5.70 ±0.66	5.83±0.24 $p_{V,S}<0.05$	0.00913±0.0052 $p_{V,S}<0.05$	74.50±7.58	0.153±0.025
SC	6.69±0.18	6.90±0.24	0.115±0.0028	68.38±3.22	0.195±0.023
VC	6.41±0.167	6.62±0.18	0.103±0.0026	70.35±1.92	0.188±0.0090

P1055(23/89) Oganov VS, Skuratova SA, Maylyan ES (USSR) Mounier Y, Lie K (France), Takacs O, Guba F, Siladi T, Ser A (Hungary).
State of female rats exposed to weightlessness during pregnancy: Physiological properties and metabolism of skeletal muscles.
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Developmental Biology; Reproductive System; Musculoskeletal System, Muscles; Metabolism
Rats; Female; Pregnant
Space Flight; COSMOS-1514. -1667

Abstract: Research on COSMOS biosatellites has established the general laws governing the effects of space flight factors on skeletal muscles in white rats. It was shown that their adaptation to weightlessness is systemic in nature, with the direction and severity of symptoms depending on the extent to which muscles are involved in the antigravity function, their functional profile, and biomechanical properties It was also established that adaptive changes in the physiological properties of the muscles that occur during space flight are accompanied by appropriate changes in muscle structure, catabolic and anabolic metabolism, and changes in some types of muscle fibers effected by reprogramming the synthesis of contractile and regulatory proteins. The changes described are biologically expedient, reversible and do not exceed the bounds of physiological adaptation.

The program to study the muscle system of pregnant rats flown on COSMOS-1514 was a logical continuation of this research, and included the following major directions:

— evaluation of the changes in contractile properties of muscle fibers;
— evaluation of the state of the system providing energy to contraction;
— evaluation of the lability of molecular composition of contractile proteins as the basis of functional adaptation of muscles.

On the day of reentry (day 18 of pregnancy) the skeletal muscles were removed from the front legs of the female rats(which had been sacrificed by decapitation): the brachial muscle (BM); medial head of the triceps (MHT), and their hind legs: the lateral and medial heads of the gastrocnemius muscle (LGM and MGM), soleus (SM); *extensor digitorum longus* (EDL); plantar muscle (PM), and also the nongravity dependent diaphragm muscle (DM).

The contractile properties of skeletal muscles were studied in preparations of glycerinized muscle fibers (bundles of 3-5 fibers) in a solution of ATP+Ca^{2+} using Szent-Gyorgyi's method as modified by the authors. The functional activity of the sarcoplasmic reticulum was studied by evaluating the mobility of Ca^{2+} ions in its membranes in the LGM, PM, and DM. A model based on caffeine contracture of single, chemically scanned muscle fibers, which had first been immersed in a solution with a high concentration of Ca^{2+} was used. Protein metabolism was studied in the BM, MHT, EDL, SM, and MGM. The concentration of total protein and of differentiated myofibrillar and soluble proteins, and the structure of myofibril proteins were investigated using electrophoresis on SDS-polyacrylic gel. Muscle bioenergetics was studied by observing rate of respiration of mitochondria in various metabolic states based on polarographic analysis of oxidative phosphorylation.

Female rats exposed to weightlessness for 5 days displayed a reliable decrease in the mass of the majority of skeletal muscles (Table 16), although relative weight of muscles was altered insignificantly. All muscles of the experimental animals, with the exception of the plantar muscle, showed a reliable decrease in strength of contraction compared to the vivarium control (Figure 16). The maximal rate of development of muscle fiber contraction in experimental

insignificantly. All muscles of the experimental animals, with the exception of the plantar muscle, showed a reliable decrease in strength of contraction compared to the vivarium control (Figure 16). The maximal rate of development of muscle fiber contraction in experimental animals was statistically significantly depressed compared with the vivarium control in preparations of all the muscles studied, with the exception of the EDL (Figure 17). The work capacity of prepared muscle fibers, which was estimated on the basis of impulse strength, was also statistically significantly depressed in preparations of the SM, MHT, and PM of the flight group, and in the BM, MGM and LGM of the flight and synchronous groups compared to the vivarium control. Thus there was a general trend toward reduction of strength, rate of contraction, and work capacity of muscle fibers, without appreciable differentiation attributable to functional profile of the muscle, as was observed after longer term space flights.

Amplitude of contraction of single muscle fibers was found to be depressed in flight animals compared to the synchronous controls in fibers of the LGM and PM. Comparison of the "stress - pCa" function revealed a decrease in the affinity of myofibrillar proteins for calcium in LGM fibers of flight animals and an increase in this parameter in rats of the synchronous group. In PM fibers the sensitivity of proteins to calcium was identical in all three groups. Mobility of Ca^{2+} in the membrane of the sarcoplasmic reticulum was estimated on the basis of amplitude of contraction after treating the fibers with caffeine. This paradigm is based on the capacity of caffeine to sharply increase the permeability of the sarcoplasmic reticulum to Ca^{2+}. The preparations were first "loaded" with calcium, i.e., kept for a period in a solution with concentration of Ca^{2+} (pCa=6.8), high enough that it does not induce direct activation of the contractile proteins. Duration of preliminary loading with calcium required to obtain maximal amplitude in a standard (contracting) solution with constant concentration of caffeine served as an indicator of the strength of calcium pumping, which in the norm is determined by the Ca-ATP-ase activity of the sarcoplasmic reticulum.

In preliminary control experiments it was shown that (within certain limits) the longer the exposure of preparations to the calcium loaded solution, the greater the amplitude of the contraction developed in response to the same dose of caffeine. Thus, with the standard dose of caffeine (5mM) duration of exposure and time to achieve maximum amplitude of contraction are functions of the strength of calcium pumping and, thus, of activity of Ca-ATP-ase of the sarcoplasmic reticulum.

The results of this experiment testify to increased intensity and rate of calcium pumping of the sarcoplasmic reticulum in muscle fibers of the LGM in rats of the synchronous control group compared to the vivarium control. The LGM of flight rats showed a decrease in rate of calcium uptake (compared to the synchronous control), with the intensity of suction unchanged. Alteration of the strength of calcium pumping in PM fibers in the flight group was analogous, but, along with decrease in rate, there was also a decrease in intensity of calcium suction.

The fact that amplitude of contraction induced by caffeine is a function of caffeine dose, given standard duration of preliminary exposure to the hypercalcic solution, reflects the capacity of the sarcoplasmic reticulum membrane to liberate calcium, since this occurs in natural initiation of contraction by a neural impulse. Results of the study show that this capacity to liberate calcium decreases somewhat in the fibers of the lateral gastrocnemius and plantar muscles of flight animals (compared to the vivarium control) and, on the other hand, increases markedly in the rats in the synchronous control group. Thus it may be concluded that in response to weightlessness, the mobility of calcium ions decreases in the membranes of the sarcoplasmic reticulum of the gastrocnemius and plantar muscles, thus decreasing their functional activity.

Tissue respiration was studied in the anterior group of muscles of the femur. Rate of mitochondrial respiration was measured in various metabolic states: substrate respiration, ADP-dependent respiration, and controlled respiration. Information was obtained about the phosphorylation function of the muscles by measuring phosphorylation (Δt) and computing parameters of energy function of the respiratory chain — respiratory control according to Lardi (RC_L) and Chancy (RC_C) — and rate of phosphorylation. The results, presented in Table 17, indicate the absence of reliable differences between the flight and vivarium control groups. Animals exposed to weightlessness for 5 days did not display any changes in mitochondrial respiration of the skeletal muscles, either in rate of oxygen loss or extent of retention of energy accumulation processes in the myocytes. At the same time animals in the synchronous control group showed changes in a number of parameters compared to the vivarium animals: decrease in ADP:O coefficient and rate of phosphorylation, increase in phosphorylation time. In the majority of cases, differences between the synchronous and flight groups were not significant. The exception was ADP:0 coefficient and rate, which was reliably lower in the synchronous than in the flight group.

No reliable differences were noted between the experimental and control groups in activity of malate dehydrogenase, isocitrate dehydrogenase, or lactate dehydrogenase in the muscle tissues of the femur. Activity of the last showed a tendency to increase, which can be considered an acute reaction associated with return to normal g. The results obtained support the idea that short-term effects of weightlessness neither induce depression of tissue respiration nor decrease its energy efficiency, despite reliable decreases in quantity of mitochondrial protein. Investigation of the composition of myofibrillar proteins, revealed no changes in the fractions of heavy chains of myosin or concentration of actin, as was also the case with flights of longer duration.

However, a decrease in concentration of light chains (LC) of myosins, particularly LC-3B, which is not normally high, at least in the SM, was observed in the SM and MHT in flight animals. Low levels of LC-3B were also established in the SM of the synchronous control group. Elevation of levels of slow isoforms of myosin light chains (particularly LC-1M) was also observed in the SM, but not the MHT. Considering that the ATP-ase activity of the myosin molecules is directly associated with the concentration of LC-3B (Weeds, Taylor, 1975), it can be concluded that the data obtained do not contradict the general direction of changes (decreases) in rate of muscle fiber contraction after a 5-day space flight. No significant changes were noted in the ratios between slow isoforms of myosin light chain in fast muscle fibers.

No appreciable changes were detected in the concentrations of individual fractions of the troponin-tropomyosin complex (TN-TM). It was notable that in the flight group, changes in the concentrations of the troponin-inhibitor complex (TN-I) of ATP-ase myosin tended to increase in fast-twitch muscles and decrease in postural muscles. An analogous tendency was observed in TN-I in the same muscles after an 18-day space flight. Thus, the results of the research suggest that short-term (5 day) space flight is accompanied in pregnant rats by appreciable changes in the contractile properties of muscle fibers, expressed in decrease in strength functions of contractile proteins, more noticeable in antigravity musculature, and in a tendency for development of the contraction process to be retarded. The results confirm the idea that the leading factor in the development of changes in postural muscles in response to weightlessness is unloading of the muscles and deficit in the tonic component of movement, as was shown for longer (18-20 day) exposure of rats to weightlessness

In addition, it was established that decrease in the strength of contraction of some muscles (SM, EDL) was incommensurate with their minimal loss of mass (Table 16; Figure 14). To explain this it is postulated that the decrease in the capacity of muscle fibers to develop force is due not only to the development of atrophy, but also to the observed decrease in the affinity of

contractile proteins for Ca^{2+}. Additional indirect evidence for this comes from the insignificant loss in myofibrillar proteins after a 5-day space flight. Comparison of the results of studies performed after two short-term space flights (COSMOS-1514 and COSMOS-1667) suggests that, after the 5-day space flight, the decrease in the strength of muscle contraction in pregnant rats applied to all muscles, while after a 7-day flight changes noted in muscles of male rats were not as marked and were in different directions in the postural and fast-twitch locomotor muscles. It may be hypothesized that more severe changes in the strength and speed properties of muscle fibers in pregnant rats after a 5-day space flight reflect factors specific to their state. Changes in the speed properties of the muscles studied and in the functional activity of the sarcoplasmic reticulum were in the same direction (decrease) for both flights.

After longer-term space flights, a statistically significant acceleration has been observed in the contraction process in the SM of rats, which is consistent with data on restructuring of the populations of myosins in this muscle. The tendency to change in the opposite direction after a 5-day flight, noted in muscle fibers, was most likely due to a decrease in Ca^{2+} mobility in membranes of the sarcoplasmic reticulum, as discussed above.

Changes noted in the function of contractile proteins of fast muscles in experimental animals after short-term space flight are, in many parameters, similar to the changes in the analogous muscles of animals in the synchronous control condition. It can be hypothesized that during this period, factors associated with the conditions under which the animals are maintained continues to play a significant role. These changes in the fast-twitch muscles are in a different direction from those occurring after longer space flights (increase in strength and speed of contraction) which the authors consider a consequence of behavioral adaptation to weightlessness.

Thus, the structural-functional and metabolic reactions of skeletal muscles described above can attest to the fact that during short-term space flight, changes in the skeletal muscles participating in the postural function are limited mainly to the level of regulation of contraction. In other words, the most sensitive components of the contraction mechanism are what suffer, although certain of the reactions observed (partial atrophy) may be adaptive in nature. Nevertheless, during this period, in all likelihood, there has not yet been a substantial restructuring of the populations of myosins and the corresponding structural profile of the muscles, such as that observed after longer-duration space flights (up to 22 days) that reflects the physiological adaptation of the muscles.

Table 16: Absolute muscle mass (mg) in female rats after a 5-day space flight

Grp	Muscles						
	BM	MHT	EDL	SM	PM	MGM	LGM
F	162.0±8.34 $p_V<0.05$ $p_S<0.05$	126.6±4.9 $p_V<0.001$ $p_S<0.01$	118.0±3.34 $p_S<0.05$	108.8±4.04 $p_S<0.05$	229.6±13.61 $p_S<0.05$	494.6±30.21 $p_V<0.05$	556.2±39.28 $p_V<0.01$ $p_S<0.01$
SC	203.4±12.18	170.611.02	142.6±4.76	131.6±8.93	278.4±16.85	555.0±30.3	731.0±23.91
VC	192.2±6.47	161.6±4.92	129.8±8.98	123.2±9.02	254.6±14.26	596.0±28.53	776.4±37.87

Table 17: Characteristics of oxidative phosphorylation in mitochondria of skeletal muscles (rate of respiration in nmole O_2/min/mg protein; substrate of oxidation 5 mM succinate)

Grp	Substrate respir.	ADP-dep. respir.	Control respir.	DKI	DKch	Δt	ADP:O	Rate of phosphor.
F	5.81±0.42	8.78±1.00	8.04±1.16	1.50±0.10	1.11±0.03	4.75±0.41	0.44±0.05 $p_S<0.001$	20.53±3.28
SC	6.85±0.62	11.55±1.34	6.42±0.70	1.68±0.10	1.86±0.31 $p_V<0.05$	5.73±0.49 $p_V<0.05$	0.28±0.02 $p_V<0.05$	18.48±2.83 $p_V<0.05$
VC	6.34±0.61	9.69±1.18	7.60±1.23	1.55±0.15	1.11±0.03	3.89±0.52	0.36±0.02	28.19±3.66

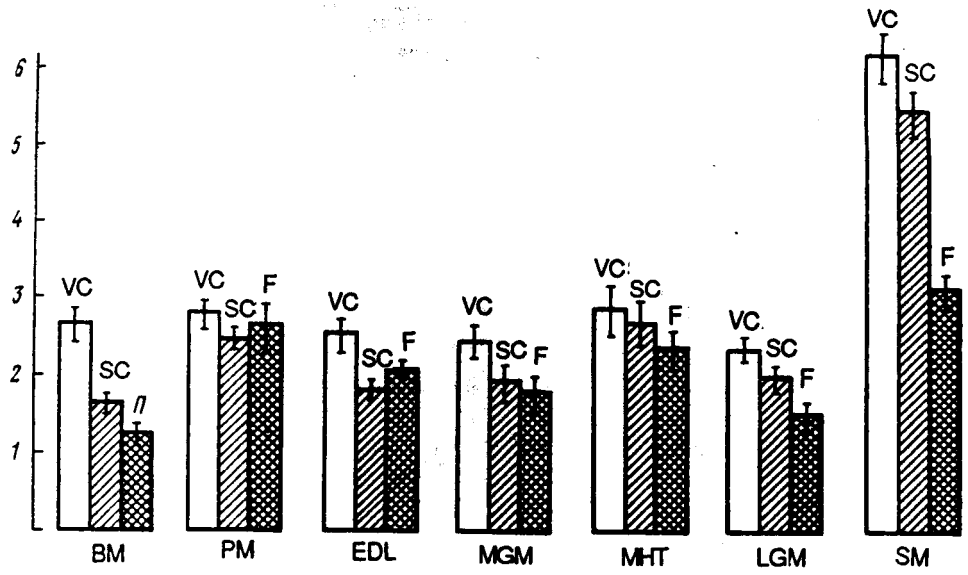

Figure 16: Changes in strength of contraction ($n \cdot mm^{-2} \cdot 10^{-1}$) of muscle fibers in female rats after space flight.

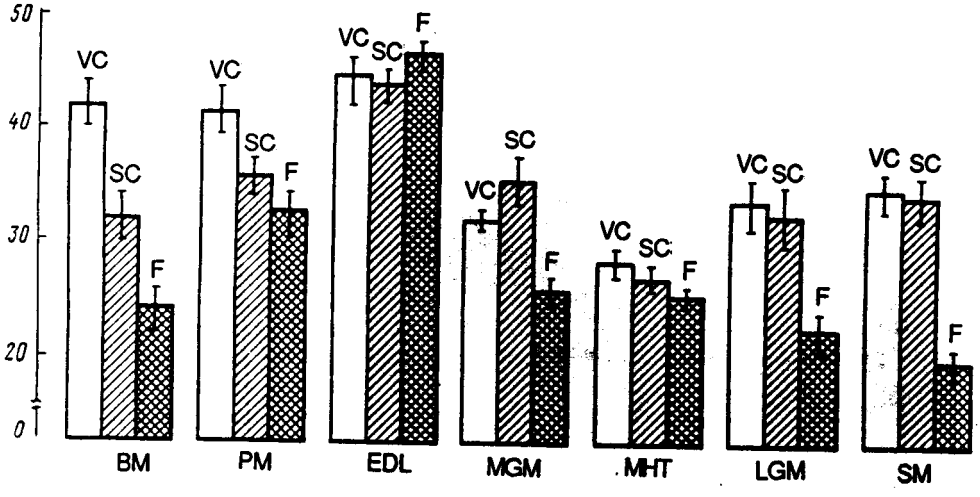

Figure 17: Change in the rate of contraction ($r \cdot sec^{-1} \cdot 10^{-3}$) of muscle fibers.

-\23/89) Baran'ska V, Kuyava M Lanchevski V, Pisarek V (Poland). Denisova LA (USSR)
State of female rats exposed to weightlessness during pregnancy: State of the ovaries.
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Developmental Biology; Reproductive System; Ovaries
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Abstract: Conclusions were drawn concerning the functional activity of the ovaries in rats exposed to weightlessness on COSMOS-1514 on days 13-18 of pregnancy, on the basis of the state of the corpus luteum, which form after ovulation if animals are pregnant and consist of a mass of cells secreting progesterone and estrogen essential for supporting the uterine endometrium in a state that allows pregnancy to continue. Unlike the case with humans, in rats the corpus luteum function until the termination of the pregnancy, participating in regulation of fetal development at all stages.

The ovaries of the rats of the flight and control groups were fixed in a 10% solution of formalin. Morphometric analysis. utilizing stereological and diffractometric methods was performed on cross sections of 8-10 μ, enclosed in paraffin and stained with hematoxylin and eosin. A total of 40 corpora lutea were analyzed for each group.

Stereological analysis of the preparations was performed using an optical microscope with magnification of 320. The volumes of the lutein and paralutein cells and their nuclei were estimated and the ratios among individual structures of the corpus luteum, lutein and paralutein cells, connective tissue and blood vessels were determined.

To evaluate the distribution of structures and their components, the experimenters performed a diffractometric analysis of preparations on photographic negatives (magnification 160: input unit 22 mm). A diffractometer with a helio-neon laser (wavelength 0.63 μm) was used. The light rays passed through the negative, underwent diffraction, and converged on the focal plain of the diffractometer, creating a diffractogram. Intensity of illumination was measured by an electron detector. Signals from the detector were amplified, differentiated, transformed, and input to a computer.

The diffractograms had a symmetrical structure, their halves were equivalent in spectral distribution, which permitted analysis in diametrically opposed geometric coordinates: one half of the layer consisted of the central ring and 31 radially arranged half rings, and the second of 32 angular spaces. Radial analysis of a portion of the diffractogram divided into half rings provided information about the sizes of the structures and the distances among them, while angular analysis in the space divided into wedges gave information about ordering in the distribution of structures.

Preparations from all flight, synchronous and vivarium control groups contained lutein and paralutein cells with typical structures (Figure 18). They were divided by connective tissue, containing, aside from cellular elements and fibers, sections of blood vessels. The qualitative morphological study of preparations revealed no differences between the corpora lutea of rats of the experimental and control groups. The stereological analysis also failed to reveal any reliable differences among the groups in the relative volume of the major components of the corpus luteum: lutein and paralutein cells, connective tissues and vessels (Table 18). When the absolute sizes of lutein cells were measured, no differences were found between the

experimental and vivarium control animals (Table 19). However, the size of the nuclei in the experimental group showed a statistically significant tendency to be depressed compared with the synchronous control (Table 19). The size of paralutein cells in the corpus luteum of animals in the flight group was the same as that of the vivarium group, but the size of their nuclei was reliably depressed. However, this parameter was even lower in the vivarium control group (Table 19). The relative volume of cell nuclei of paralutein cells was reliably depressed in the experimental group compared to that of the two control groups (Table 20).

The results of angular analysis of the diffractogram support the idea of a normal distribution of structures in the elements of the corpus luteum of animals of all three groups. The absence of differences between the experimental and control animals in localization of diffractogram maxima indicates similarity in the ordering of structures. Discriminant angular analysis failed to reveal reliable differences between groups.

Figure 19 presents the results of radial analysis of the diffractogram. Analysis of the decomposition of light intensity among the half rings attests to the heterogeneity of the sizes of structures of the corpus luteum in animals of all three groups. Distribution of maxima in individual half-rings was the same for experimental and control groups; however, the greatest maximum for animals of the flight group was displaced to the left compared with the vivarium control group and there was some displacement in the synchronous group as well. This may indicate that the individual components of the corpus luteum were of different sizes for the experimental and control groups. Discriminant analysis was performed to identify reliable differences. When decomposition of the light was compared in the 32 half rings using discriminant analysis techniques, the greatest differences were found in half rings 1, 2, 22, 29, and 30. Decomposition of the light in half rings 1 and 2, according to the theory of Fourier transforms, corresponds to parameters indicative of the optical density of the entire sample, which, depends, to a significant extent, on the processes of fixation and staining and on subsequent photographic processing of the negative; for this reason these differences were not considered. Statistically significant differences ($p<0.05$) were found in half rings 19, 22, 24, 29, and 30, corresponding to elements of the corpus luteum, with dimensions in the ranges of 0.7-0.8 μm.

Comparing the results of diffractometric and stereological analyses, one might postulate that differences identified using diffractometry are associated with changes in the state of paralutein cells, which had nuclei that are reliably smaller in animals of the flight group, than those in the vivarium and synchronous control groups (Table 19). The corpus luteum is a temporary organ. At the termination of pregnancy, when the functioning of the placenta reaches a maximum, the functional activity of corpus luteum decreases and the differences observed here may be a sign of differences in cellular degeneration of paralutein cells in the animals of the different groups caused by differences in the hormonal status and metabolism of rats in the flight group as described above.

Table 18: Relative sizes of components of the corpus luteum, %

Group	Lutein cells	Paralutein cells	Connective tissue	Blood vessels
F	41.78±2.20	35.06±2.14	16.87±0.56	2.39±0.29
SC	47.56±2.04	30.04±2.16	16.36±0.60	2.38±0.28
VC	46.96±2.04	28.47±1.94	17.21±0.65	2.60±0.33

Table 19: The size (mm^3) of lutein and paralutein cells and their nuclei

Group	Lutein cells		Paralutein cells	
	Cells	Nuclei	Cells	Nuclei
F	2950±171	300.34±17.45	1036.8±43.2	142.04±4.67
		$p_S<0.05$		$p_{V,S}<0.05$
SC	3454±186	369.94±19.9	642.3±30.2	99.43±4.67
			$p_{V,S}<0.05$	$p_V<0.05$
VC	3218±248	325.74±25.1	966.7±48.4	176.33±8.82

Table 20: Relative size (%) of nuclei of corpus luteum cells

Group	Lutein cells	Paralutein cells
F	10.18±0.44	13.7±0.63
		$p_{V,S}<0.05$
SC	10.71±0.65	15.48±0.64
VC	10.12±0.5	18.24±0.93

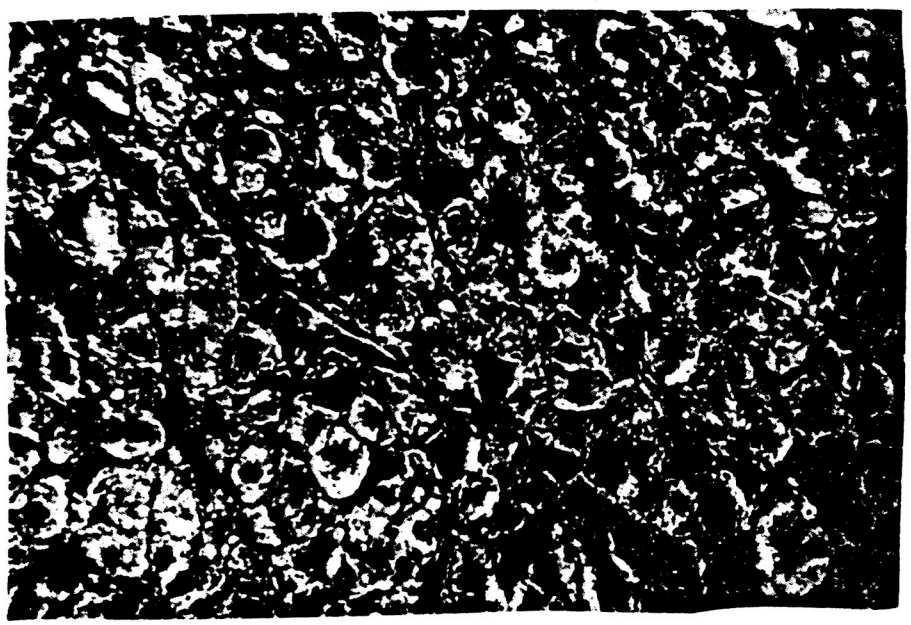

Figure 18: Fragment of the corpus luteum of a female rat of the flight group. Mag. 350

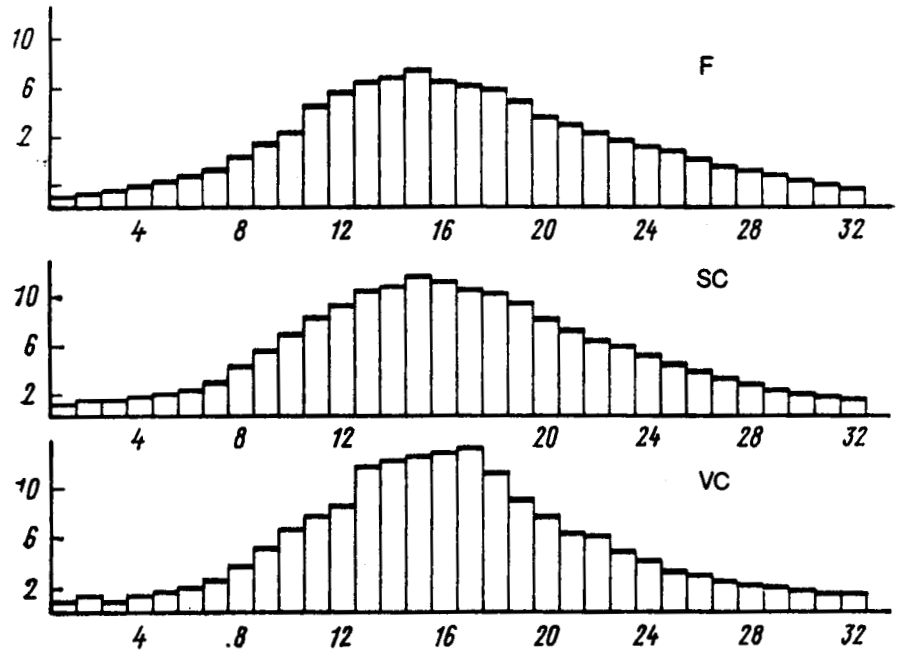

Figure 19: Radial analysis of elements of the corpus luteum. Distribution of light intensity among half rings

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16. Abstract

This is the twenty-third issue of NASA's USSR Space Life Sciences Digest. It contains abstracts of 47 journal papers or book chapters published in Russian and of five Soviet monographs and one book review. Selected abstracts are illustrated with figures and tables from the original. A special feature provides a translation of a discussion on biomedical support of manned flights to Mars. The abstracts in this issue have been identified as relevant to 32 areas of space biology and medicine. These areas are: adaptation, aviation medicine, biological rhythms, biospherics, body fluids, botany, cardiovascular and respiratory systems, cytology, developmental biology, endocrinology, enzymology, equipment and instrumentation, gastrointestinal system, genetics, group dynamics, habitability and environmental effects, hematology, human performance, immunology, life support systems, man-machine systems, mathematical modeling, metabolism, microbiology, musculoskeletal system, neurophysiology, nutrition, operational medicine, perception, psychology, radiobiology, and reproductive system.

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